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# Progesterone Therapy for Menopause

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## Article |

## Progesterone Therapy for Menopause

by Dr. Jerilynn C. Prior, Scientific Director, Centre for Menstrual Cycle and Ovulation Research

“Bio-identical” is the trendy term for therapies we've used for a long time. Bio-identical therapies include Prometrium<sup>®</sup>, Estrace<sup>®</sup>, Estradot<sup>®</sup>, Androgel<sup>®</sup>, Climara<sup>®</sup> and Estragel<sup>®</sup> to list a few examples. It simply means hormonal therapies that are identical to ones that the human body makes.

The purpose of this article is to highlight the ways in which *oral micronized progesterone* therapy (taken by mouth as a pill) can be helpful for menopausal women with hot flashes, sleep disturbances or osteoporosis (menopause being one year after all flow has ceased). A second purpose is to identify the relative safety of progesterone (in contrast to the diseases that menopausal estrogen treatment causes). Rather than progesterone in general, this article focuses on *oral micronized progesterone* (hereafter just called Oral Progesterone) that is manufactured as Prometrium<sup>®</sup> or can be compounded in olive or safflower oil as a capsule by local pharmacies. The advantages of Oral Progesterone are that blood levels from a given dose are known and that it increases deep sleep. The dose of 300 mg at bedtime keeps the progesterone blood level in normal ranges for the normal menstrual cycle's luteal phase (after ovulation) range for 24 hours. The main problem with progesterone creams is that they have not yet been sufficiently standardized so that we know what doses correspond to what progesterone blood levels. A second problem is that the creams don't help sleep as Oral Progesterone does.

This article is about Oral Progesterone as a *therapy* that is to be taken daily by symptomatic menopausal women who need treatment. I am not saying that it is normal to have high progesterone levels after menopause any more than it is normal to have high estrogen levels. In nature, except during pregnancy, progesterone is high only for two weeks at a time in menstruating premenopausal women.

### Why treat Menopausal Women with Oral Micronized Progesterone?

The most important reason for using Oral Progesterone is for the treatment of hot flashes and night sweats. Since the 1970s, many progestins (synthetic cousins of progesterone), especially medroxyprogesterone (20 mg/d) have been proven to be effective treatment for hot flashes (1;2 [1]). One progestin called Megestrol (Megace<sup>®</sup>) that is used in women with advanced breast cancer decreased hot flashes by 83% over only one month (3 [2]). Progesterone *cream* in a dose of 40 mg decreased hot flashes significantly more than placebo in a one-year study (4). However, 32 mg once a day in a shorter study did not (5 [3]).

Ironically, we have information about the effectiveness of progestins and progesterone cream, yet so far we have nothing published about Oral Progesterone. For that reason, CeMCOR is currently performing the first randomized, double blind placebo-controlled trial of Prometrium ® for night sweats and hot flushes. (To learn more about this reasearch study, [click here](#) [4] [5]).

Based on clinical experience, CeMCOR also recommends using Oral Progesterone to help menopausal women wishing to stop estrogen treatment. Women with past hot flushes who are on estrogen treatment can gradually discontinue that therapy and, by taking Oral Progesterone, not get severe flushes again. (For more information on this, read [Stopping Estrogen Treatment](#) [6]).

A second reason for using Oral Progesterone therapy is for sleep disturbances. Lack of adequate sleep is not uncommon for menopausal women and this lack of sleep is linked to physical and emotional problems. Interestingly, studies of Prometrium ® and sleep have been performed in men but not in women! The men's sleep study documented the phases of sleep in a sleep laboratory by treatment with Prometrium ® 300 mg at bedtime or placebo ([6](#) [7]). This study showed that Oral Progesterone increased deep sleep by approximately 15 percent. Because Oral Progesterone causes deep sleep without risks for addiction, without suppression of breathing control (like all other powerful sedatives) and with no decrease in restorative rapid eye movement (REM) sleep, it is safer than all the sleeping pills currently available.

The third reason for using Oral Progesterone treatment for menopausal women is to assist in the treatment of osteoporosis. Progesterone stimulates formation of new bone ([7](#) [8]). Normal cyclic progesterone levels, for example, are necessary to prevent bone loss in healthy premenopausal women ages 20-40 with regular menstrual cycles and normal estrogen levels ([8](#) [9]). A study of cyclic medroxyprogesterone and calcium (or placebos) in physically active premenopausal women with mixed up periods showed a highly significant increase in spine bone density in the women getting medroxyprogesterone and an important but not quite significant effect of the extra calcium ([9](#) [10]). A recent randomized controlled trial in menopausal women showed that very low dose medroxyprogesterone added to estrogen caused a significant 1-2% greater increase in spinal bone over two years than that caused by estrogen alone ([10](#) [11]). A preliminary study also indicated that Oral Progesterone or medroxyprogesterone added to the positive effect of the bisphosphonate, Etidronate, on spine and hip bone densities ([11](#) [12]). Whether or not Oral Progesterone will add to fracture prevention, when given together with therapies that decrease bone loss, is not yet known. By itself Oral Progesterone will not create new bone unless rates of bone loss are normal.

### **Is Oral Micronized Progesterone Therapy Safe?**

The short answer is Yes! Oral Progesterone is safe. Right now is a time of very natural skepticism — after all, didn't the experts tell us that estrogen was safe and prevented heart attacks and Alzheimer's disease? And now we know the opposite is true ([12](#) [13]). How can I be sure that Oral Progesterone is safe when the Canadian Pharmaceutical Compendium ([13](#) [14]) and other drug reference books refer to a potential for it to cause abnormal vaginal bleeding, blood clots and to possibly increase the risk for breast cancer? The strongest evidence that progesterone does not cause harm comes from the very high levels of progesterone during pregnancy. As one of my patients said, "The Great Mother wouldn't expose a fetus to high levels of progesterone if it weren't safe!"

The most common side effect of Oral Progesterone is sleepiness, which is why it helps with sleep problems as described above. It can also cause a woozy or dizzy feeling (if you wake to go to the washroom within a couple of hours of taking it). It must not be taken when awake or if driving or operating machinery. Progesterone increases flow through small blood vessels ([14](#) [15]) in a similar way as estrogen. It decreases blood pressure ([15](#) [16]). It increases the rate of breathing and therefore is helpful for some lung diseases. It also causes us to burn about 300 more calories a day ([16](#) [17]) because it increases our basal body temperature. And it blocks the production of dihydrotestosterone, the male hormone that causes acne and

unwanted facial hair growth (17 [18]). Progesterone is used to prevent and treat endometrial cancer. And two randomized, placebo-controlled studies in women suggest that progesterone decreases breast cell growth that is linked to breast cancer (18; 19 [19]). Very large randomized controlled trials of Oral Progesterone and placebo have not yet been performed, however.

In day-to-day life the major “side effect” of Prometrium® is its cost, which is about \$2.00 a day for the 300-mg dose that is optimal for hot flushes, sleep and bone formation. The compounded Oral Progesterone, in a 300-mg capsule with olive oil, is significantly less expensive at about \$1.00 a day.

### **How should I Take Oral Micronized Progesterone?**

Instructions for menopausal Oral Progesterone treatment are similar to those for pre- and perimenopausal women Cyclic Progesterone Therapy [20] except that the 300-mg dose is taken *every day*. Take a compounded oral micronized progesterone, rather than Prometrium® if you are allergic to peanuts because it is dissolved in peanut oil. Progesterone should be taken *on the way to bed*. Then the drowsy side effects become helpful for sleep.

### **Are there things I should watch for on Oral Micronized Progesterone Treatment?**

Women with liver failure (jaundice, fluid in the abdomen called ascites and very abnormal liver blood tests) should avoid Oral Progesterone. It is highly unusual to have vaginal bleeding or spotting on progesterone or medroxyprogesterone taken without estrogen. Sometimes, the endometrium (lining of the uterus) was thickened by past estrogen treatment or because of being overweight or perhaps having Type-2 diabetes. If any of those factors might apply to you, and you are just starting Oral Progesterone, take it for 14 days and then stop it for three to five days. If there is any lining to shed you will have some flow during those first days off Oral Progesterone. You can re-start Oral Progesterone with an extremely low risk for further bleeding.

Although Oral Progesterone is an effective treatment for endometrial cancer and does not cause it, if you have any spotting or bleeding while taking it every night, make sure that you are not also taking any kind of estrogen. That means you are not using a vaginal estrogen cream, or estrogen-like herbal products (isoflavone pills, black cohosh or Remifemin®). Because bleeding after menopause could mean cancer, an endometrial biopsy is usually needed.

### **How long should I take Oral Micronized Progesterone Therapy?**

In general the answer is “As long as you need it.” For women with hot flushes/night sweats, it is useful to try tapering off the Oral Progesterone once a year. For sleep disturbances you can do the same. For Oral Progesterone as an osteoporosis co-treatment with therapy preventing bone loss, I'd recommend taking it for at least five years. Physiology suggests that it is safe for longer periods of time but no long-term studies have yet been performed.

### **Summary — Menopausal Oral Micronized Progesterone Therapy**

Three hundred milligrams of Oral Progesterone treatment at bedtime daily is useful for menopausal women with night sweats, hot flushes, sleep disturbances and osteoporosis. Oral Progesterone also helps women to stop estrogen without experiencing recurrent severe hot flushes. Those taking Oral Progesterone can safely continue it for as long as they need it. Symptomatic menopausal women are asking for effective, safe and bio-identical hormonal therapy. Oral Micronized Progesterone fits that bill.

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