

PATIENT HANDOUT

Natural Progesterone



What is progesterone?

- Progesterone (proe-JES-ter-one) is one of several sex hormones made by the human body. Other sex hormones produced by the body include estrogen, estradiol, estriol, and testosterone.
- In women, progesterone is produced by the ovaries. Progesterone helps to regulate the menstrual cycle and is necessary to sustain a pregnancy.
 - An increase in progesterone level leads to a build-up in the lining of the endometrium, the inner part of the uterus, preparing the uterus for implantation of a fertilized egg. The progesterone level decreases when fertilization does not occur, leading to shedding of the uterine lining as menstruation.
 - An increase in progesterone level also is responsible for signaling the mammary glands to produce milk.
- Progesterone is produced naturally in the body. There are several synthetic forms of progesterone, called progestins, which are manufactured and are not found naturally in the human body. Progestins are the type of progesterone found in most commercially available hormone replacement products and birth control pills.

Why do we need to supplement the body's natural production of progesterone?

- As women enter menopause, their levels of progesterone and other sex hormones decrease. This often leads to unwanted symptoms such as hot flashes, vaginal dryness, breast tenderness, low libido, depression, anxiety, food cravings, insomnia, cramps, emotional swings, weight gain, and bloating. Because of these effects, some women choose to supplement their levels of sex hormones by taking hormone replacement therapy.
- The decision to begin hormone replacement therapy should be made after careful discussion with your doctor and pharmacist. There are both benefits and risks to taking hormone replacement therapy that should be weighed before you begin a hormone replacement regimen. Each woman is different, and the right decision for one woman may not be the right decision for another.

What is progesterone's role in hormone replacement therapy?

- Aids in the function of thyroid hormone
- Helps maintain sex drive
- Improves mood
- May help relieve hot flashes
- Protects against and helps reverse osteoporosis
- Protects against breast cancer and endometrial cancer

Who should avoid taking progesterone?

- If you have any of these conditions, you should not take progesterone without discussing it with your doctor and pharmacist:
 - Allergy to progesterone
 - Arterial disease (or high risk for arterial disease)
 - Liver disease
 - Major depression
 - Pregnancy (although some women with low natural levels of progesterone may be given progesterone during pregnancy)
 - Vaginal bleeding of unknown cause
- Women who have any of the following diseases may experience fluid retention from progesterone:
 - Asthma
 - Cardiovascular disease
 - Diabetes mellitus
 - Epilepsy
 - Kidney dysfunction
 - Migraines

What are the available dosage forms of progesterone?

- Injection
- Oral capsules, tablets, or liquid
- Topical cream or gel
 - If you are using topical progesterone, avoid skin-to-skin contact with others for at least 30 minutes.
- Troches (lozenges that melt under the tongue)
- Vaginal suppository

How is progesterone different from the progestins?

- Unlike progesterone, which is made by the body, progestins are commercially prepared chemicals that are not identical to those made naturally by the body.
- Because of this, side effects of progesterone and progestins differ in type and severity.
 - Progestins
 - Synthetic progestins increase the level of low-density lipoprotein (LDL), or “bad,” cholesterol, and decrease the level of high-density lipoprotein (HDL), or “good,” cholesterol—and thus can increase a woman's risk of developing atherosclerosis (hardening of the arteries).
 - Other side effects of synthetic progestins include abdominal bloating, breast discomfort, headache, depression, weight gain, and acne.

- Progesterone
 - Progesterone is unlikely to increase blood cholesterol levels and is better than progestins at preventing menopause-related changes in cholesterol levels.
 - Progesterone is less likely to cause breast tenderness, fluid retention, headache, and liver disease than progestins.
 - The only significant side effect associated with progesterone is drowsiness.
- Recent clinical trials suggest that progestins may have a detrimental effect on your health, increasing your risk of cardiovascular disease and dementia. While most of these studies have not investigated progesterone, those that have involved progesterone indicate that progesterone may not have the same detrimental effects as progestins.

How do the large clinical trials on hormone replacement therapy apply to progesterone?

- Most clinical trials have studied progestins, not progesterone.
- The Postmenopausal Estrogen/Progestin Interventions (PEPI) trial, whose results were published in 1995, studied women taking estrogen alone, estrogen plus progesterone, or estrogen plus a progestin. The researchers determined that women taking estrogen alone had better cholesterol levels than when they began taking the estrogen. Those who took estrogen and progesterone had about the same positive effect on cholesterol. Estrogen and a progestin did not have as much of a cholesterol-lowering effect as estrogen and progesterone, suggesting that progestins may have an adverse effect on cardiovascular health.
- The Women's Health Initiative (WHI) trial is a large-scale study involving thousands of women on hormone replacement therapy. In July of 2002, one part of this trial was ended early by the researchers because they found that women taking the study hormones had significantly higher risks of several undesirable conditions than women taking placebo (sugar

pill). The hormone combination being investigated in this part of the study included conjugated estrogens and progestin. Neither conjugated estrogens nor progestins are found naturally in a woman's body, but they are the active ingredients in several commercial hormone products. The women taking hormones in this part of the study had higher risks of stroke, heart attack, dementia, and breast cancer that was difficult to detect by mammography.

- It is important to remember that progesterone was not involved in the WHI trial, so we cannot say that these increased risks would also apply to women taking progesterone.

What can compounding pharmacists provide for hormone replacement therapy?

- Compounding pharmacists use natural progesterone to formulate bioidentical hormone replacement therapy (BHRT). BHRT offers a safer, more natural alternative to synthetic progestins.
- Only one commercial preparation (Prometrium) contains natural progesterone, and it is available only as capsules in two doses. Women who require a different dosage form or strength can benefit from the expertise of a compounding pharmacist.
- BHRT is available in many dosage forms to suit your preferences. Compounding pharmacists work with your physician to individualize treatment to your needs.
- Women who cannot tolerate oral progesterone, for example, may benefit from a topical preparation or a vaginal suppository.

The International Journal of Pharmaceutical Compounding wishes to acknowledge Rachael Kuntz, PharmD, as the author of this handout.