

Statistically significant improvements in premenstrual syndrome (PMS) symptoms and hormone balance.

Clinical Trial: PMS

Results of a clinical trial of 40 PMS patients between ages 21-45 on the Estrium program for two menstrual cycles:¹

59% Reduction in PMS Symptoms

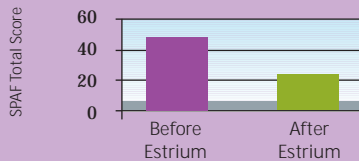


Figure 1. Clinical evaluation for PMS, as scored by the Shortened Premenstrual Assessment Form* (SPAF), showed a significant improvement in symptoms.

Improved Serum Estradiol & Progesterone

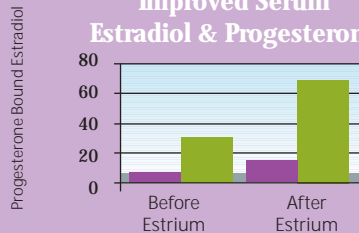


Figure 2. Subjects demonstrated a significant increase ($p < 0.002$) in mean serum levels of bound estradiol, from 31.3 to 63.7 (reference range: < 60 pg/mL). And a significant increase ($p < 0.005$) in mean serum levels of progesterone, from 4.1 to 10.2 (reference range: < 10 mg/mL).

Improved Estrogen Excretion

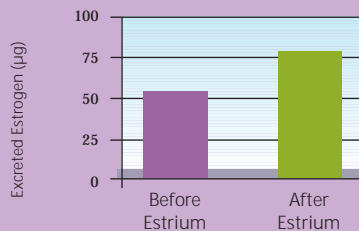


Figure 3. The subjects' average estrogen excretion over a 24-hour period also significantly improved ($p < 0.005$), from 53.5 to 77.6 (reference range: 18-62 µg).

*The Shortened Premenstrual Assessment Form (SPAF) rates symptoms in the last half of a woman's cycle, including pain, affect, and water retention. Scores range from 10 to 60; scores above 30 indicate symptomatology.

EstriumTM

Medical Food (formerly EstroBalanceTM)

Clinically Tested, Advanced Nutritional Support for Healthy Hormone Balance

Patient Benefits:

- Specially formulated to support patients with symptoms or conditions associated with hormone imbalance, including:
 - ▶ Abdominal discomfort
 - ▶ Breast tenderness
 - ▶ Feeling sad or blue
 - ▶ Joint stiffness
 - ▶ Water retention
 - ▶ Minor muscle pain
 - ▶ Feeling bloated
 - ▶ Occasional irritability
 - ▶ Temporary weight gain
 - ▶ Swelling
- Provides a scientifically designed blend of nutrients to:
 - ▶ Promote healthy hormone cycles
 - ▶ Relieve symptoms of premenstrual syndrome (PMS)
 - ▶ Address silent issues of hormone imbalance
 - ▶ Promote healthy estrogen metabolism and excretion
 - ▶ Modify the effects of circulating estrogens
 - ▶ Reduce PMS symptomatology during perimenopause and menopause
- Comes with step-by-step Patient Guide with instructions and dietary recommendations
- New **Tropical Mango** flavor! Delicious natural flavor (with new mixing variations) to encourage patient compliance

Thousands of healthcare practitioners worldwide trust clinically tested Estrium as the cornerstone of therapeutic programs to support healthy hormone balance.

Scientifically formulated, clinically tested Estrium.

RESULTS OF CASE STUDIES

Case study[†]: PMS and Endometriosis

A 36-year old Caucasian female presented with a prior diagnosis of endometriosis. Her symptoms started at about age 30 and included significant premenstrual syndrome (PMS) and painful, long menstrual periods lasting 7-10 days. The patient also reported having cramps, increased menstrual flow, nausea, and alternating diarrhea and constipation.²

85% Improvement in General Physical Symptoms

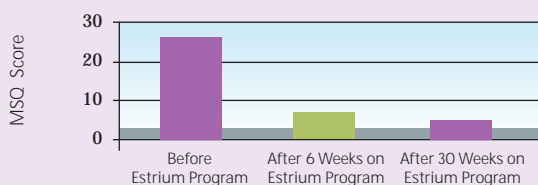


Figure 4. A substantial improvement was observed in general physical symptoms as assessed by the MSQ[®] questionnaire (reference range: <30 = few or low intensity symptoms). The patient's MSQ score was assessed initially, at 6 weeks, and at 30 weeks.

Case study[†]: PMS

A 40-year-old female presented with PMS symptoms that had been constant since the onset of menses at age 13. The patient's symptoms were predominant during the second half of her cycle and included breast tenderness, bloating, mood swings, depression, and anxiety.³

66% Reduction in PMS Symptoms

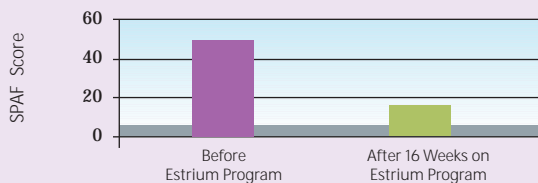


Figure 5. After just 16 weeks on Estrium, the patient's SPAF score decreased from 50 to 17 (reference range: 30 = few or low intensity symptoms). This result suggests a considerable improvement in PMS symptoms.

41% Improvement in Mental Functioning Scores

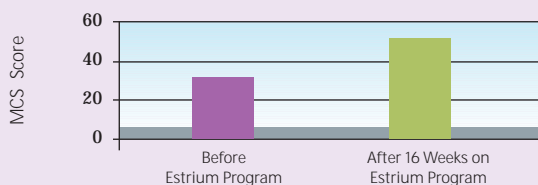


Figure 6. The patient's MCS^{**} score (reference range: 50 or above = healthy function) increased from 31.8 to 53.6 over the course of 16 weeks. This result suggests a noteworthy improvement in mental functioning.

[†]Note: The information provided in each Case Study above describes the results of one patient under the care of a licensed healthcare practitioner and may not be a typical response.

WHAT SETS ESTRIUM APART?

- **Clinically tested.** Clinical and case studies conducted at the Functional Medicine Research CenterSM—the research arm of Metagenics—demonstrate safety and efficacy.
- **History of use.** In addition to specific human research, thousands of clinicians and their patients worldwide have experienced reliable results.
- **Non-soy phytoestrogens.** Non-soy isoflavones from kudzu and lignans from flax modify the effects of circulating estrogens.^{4,6}
- **Detoxification nutrients.** Curcumin is an active component of turmeric shown to play a role in detoxification and demonstrated in vitro to reduce xenoestrogen-induced growth of cancer cells.⁷⁻⁹ N-acetylcysteine, an amino acid used for the synthesis of glutathione, supports the glutathione conjugation detoxification pathway. It also supports Phase II sulfation—an important step in estrogen detoxification.^{10,11}
- **Targeted vitamins and minerals.** Magnesium, calcium, and vitamin E are associated with significant improvements in premenstrual symptoms.¹²⁻¹⁴ Choline, trimethylglycine, folic acid, and vitamins B₂, B₆, and B₁₂ support healthy methylation pathways that are important to the health of estrogen-sensitive tissues and overall wellness.¹⁵ Additionally, high B₆ levels have been shown to attenuate an increased estrogenic response in vitro.¹⁶
- **Free of common allergens.** Free of dairy products, soy protein, gluten, wheat, egg, yeast, and artificial flavors, sweeteners, and colors.
- **Low-allergy-potential rice protein.** Derived from a patented process, Estrium contains rice protein concentrate with a lower allergy potential than normal rice.¹⁷ Fortified with the amino acids threonine and lysine, Estrium provides a complete, easily digested source of protein.
- **Easy to use.** A nutrient-dense, powdered form allows for easy mixing with juice, milk, or milk alternatives for a great-tasting beverage.

^{*}The Medical Symptoms Questionnaire[®] (MSQ) is a clinical tool for the evaluation of general physical symptoms. Total scores above 75 are generally associated with substantial symptomatology and disability; scores below 30 generally indicate few or low intensity symptoms.

^{**}The Medical Outcomes Survey SF-36 is a well-validated general quality-of-life questionnaire that summarizes health outcome in two reliable reproducible scores: the Physical Component Summary (PCS) and the Mental Component Summary (MCS). Scores above 50 or higher are associated with healthier individuals, whereas scores lower than 50 indicate compromised functioning.

THE ESTRIUM PROGRAM

Estrium is formulated to support women throughout all phases of their adult lives. The Estrium Program consists of Estrium along with a specialized dietary plan—making it a total program for healthy hormone balance. While Estrium nutritionally supports hormone balance and helps relieve hormone-related symptoms, the Estrium patient materials and educational resources target lifestyle challenges and help women transform their eating habits.



The Estrium Program incorporates a new, simplified dietary plan to nutritionally support the management of hormone-related symptoms and promote optimal hormone balance.

Implementation: Patients consume 1 serving of Estrium for breakfast or as a mid-morning snack and another as a mid-afternoon snack daily. They can select from beverage recipes in the new Estrium Patient Guide. Patients follow the Estrium dietary guidelines as closely as possible. Sample recipes are included, along with a shopping list and tips for dining out.

Maintenance Program: When your patient completes the initial phase of the Estrium Program (generally within 8 weeks), it is suggested you meet with her for an evaluation. At that point, you may recommend that she continue on the program, continue Estrium or the diet alone, or use some other combination of diet and nutritional supplementation.

Additional Support for Hormone Balance:

Clinically tested EstroFactors™ is an advanced nutritional supplement to support hormone balance—in convenient tablet form—that may be used as transitional support following the Estrium Program as women start to adopt healthy eating patterns to sustain optimal hormone balance.♦

Successfully used by women of all ages, EstroFactors has also been clinically tested in menopausal women and shown to:♦¹⁸

- Relieve hot flashes/night sweats and mild mood swings.
- Promote the conversion of estrone to 2-hydroxyestrone, a weak estrogen that may protect breast tissue.

EstroFactors features non-soy isoflavones, active folates, and other targeted phytonutrients in a formula designed to support multiple factors of estrogen activity and metabolism. Use of this essential women's health formula may improve symptoms of PMS, perimenopause, and menopause.♦

♦ These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

PROGRAM MATERIALS

- **Patient Guide.** This comprehensive program guide contains menus, recipes, and helpful FAQs.
- **Patient Education Card.** Patient-friendly office collateral.
- **Metagenics.com.** Online reference tool featuring recipes for the dietary plan and more.

For More Information on Estrogen Metabolism and Estrium

- **Applied Nutrition Science Review (ANSR) Article.** "Nutritional Influences on Estrogen Metabolism." A technical review of hormone imbalance and natural treatments for cycle-related symptoms.
- **Case Studies.** Individual case management studies demonstrate the effectiveness of the Estrium Program in a clinical setting.



Estrium

Nutrient Profile:

| Caloric Distribution | Percent of Total Energy |
|----------------------|-------------------------|
| Protein | 38% of calories |
| Carbohydrate | 45% of calories |
| Fat | 17% of calories |

Nutritional Information Per Serving:

| | |
|------------------------------|-----------------|
| Serving size | 2 scoops (45 g) |
| Servings per container | 14 |
| Calories | 160 |
| Fat | 4 g |
| Cholesterol* | 0 mg |
| Sodium | 50 mg |
| Potassium | 350 mg |
| Total Carbohydrate | 22 g |
| Simple | 12 g |
| Complex | 5 g |
| Dietary Fiber | 5 g |
| Protein | 15 g |

Each Serving Contains:

| | % RDI |
|---|------------------|
| Vitamin A (as retinyl palmitate) | 1250 IU25 |
| Vitamin A (as mixed carotenoids) | 2500 IU50 |
| Vitamin C (as Ultra Potent-C®) | 60 mg100 |
| Vitamin D (as cholecalciferol) | 200 IU50 |
| Vitamin E (as d-alpha tocopheryl succinate) | 300 IU1000 |
| Vitamin K | 40 mcg 50 |
| Thiamin (as thiamin hydrochloride) | 0.75 mg50 |
| Riboflavin | 0.85 mg50 |
| Niacin (as niacinamide) | 10 mg50 |
| Vitamin B ₆ (as pyridoxine hydrochloride) | 50 mg2500 |
| Folate (as folic acid) | 500 mcg125 |
| Vitamin B ₁₂ (as cyanocobalamin, methylcobalamin) | 30 mcg500 |
| Biotin | 150 mcg50 |
| Pantothenic Acid (as D-calcium pantothenate) | 5 mg50 |
| Calcium (as calcium citrate) | 350 mg35 |
| Iron (as ferrochel amino acid chelate [†]) | 9 mg50 |
| Phosphorus | 260 mg25 |
| Iodine (as potassium iodide) | 75 mcg50 |
| Magnesium (as magnesium bis-glycinate ^{††} , citrate) | 240 mg60 |
| Zinc (as zinc citrate) | 7.5 mg50 |
| Selenium (as amino acid complex) | 35 mcg50 |
| Copper (as copper citrate) | 1 mg50 |
| Manganese | 1 mg50 |
| Chromium (as chromium polynicotinate) | 100 mcg83 |
| Molybdenum (as amino acid chelate) | 37.5 mcg50 |
| L-Lysine | 17.5 mg** |
| L-Threonine | 17.5 mg** |
| Isoflavones (from kudzu) | 25 mg** |
| Defatted Flaxseed Meal | 1 g** |
| Choline (as choline bitartrate) | 250 mg** |
| Tumeric Rhizome Extract (Curcuma longa) | 210 mg** |
| [standardized to 95% (200 mg) curcuminoids] | |
| Trimethylglycine | 200 mg** |
| N-Acetylcysteine | 100 mg** |

Other Ingredients: Rice protein concentrate, rice syrup solids, fructose, olive oil, natural flavors, xanthan, carrageenan, cellulose gum, pueraria root extract.

Directions: Blend or shake 2 level scoops (45 grams) of Estrium into 8 ounces of juice; soy, almond, rice, or organic cow's milk; water; or as directed.

Form: 22.2 oz. (630 g) Powder Container (14 Servings)

References:

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Estrium medical food is researched, developed, and manufactured by Metagenics, Inc.

[†]Information on cholesterol content is provided for individuals, who, on the advice of a physician, are modifying their dietary intake of cholesterol.

^{††}The U.S. RDI has not been established for this nutrient.

^{†††}Ultra Potent-C® is a registered trademark of Metagenics, Inc. U.S. Patent #5,626,883.

^{††††}As MetaMag™, our proprietary fully reacted magnesium amino acid chelate: U.S. Patent Nos. 4,830,716; 4,599,152 Albion®

Production of the rice protein is covered by U.S. Patent #4,876,096.



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