PART III: CONSUMER INFORMATION

PROMETRIUM®
Progesterone capsules

This leaflet is part III of a three-part "Product Monograph" published when PROMETRIUM® was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about PROMETRIUM®. Contact your doctor or pharmacist if you have any questions about the drug.

Please read this CONSUMER INFORMATION carefully before you start taking PROMETRIUM® and each time you have your prescription refilled. It contains information on what PROMETRIUM® is, when and how to take it, what to look out for, and some information regarding possible risks of hormone replacement therapy obtained from the results of the Women's Health Initiative Study. This information leaflet does not take the place of talking to your healthcare provider about your medical condition or your treatment.

ABOUT THIS MEDICATION

What the medication is used for:
PROMETRIUM® (micronized progesterone) is approved for use in the following situation:

- In women with an intact uterus (have not had surgery to remove the uterus) who are using estrogen replacement therapy for menopause

Progesterone, as in PROMETRIUM® capsules, has a strong influence on the inner lining of the uterus and is used with estrogen therapy during and after menopause. The purpose of using progesterone is to protect the inner lining of the uterus from overgrowth caused by estrogen therapy.

PROMETRIUM® should be used only under the supervision of a doctor, with regular follow-up at least once a year to identify side effects associated with its use. Your first follow-up visit should be within 3 to 6 months of starting treatment. Your visit may include a blood pressure check, a breast exam, a Pap smear and pelvic exam. You should have a mammogram before starting treatment and at regular intervals as recommended by your doctor. Your doctor may recommend some blood tests.

You should carefully discuss the risks and benefits of hormone replacement therapy (HRT) with your doctor. You should regularly talk with your doctor about whether you still need treatment with HRT.

What it does:
The active ingredient in PROMETRIUM® capsules is progesterone, a natural female hormone. In healthy women of childbearing age, progesterone is produced by the ovaries each month during the second part of the menstrual cycle. Progesterone plays a role in the monthly shedding of the inner lining of the uterus (endometrium) and the menstrual bleeding that follows.

When it should not be used:
Do not use PROMETRIUM® (micronized progesterone) if you:

- Have an allergic or an unusual reaction to progesterone, soya, peanut or to any of the ingredients in PROMETRIUM®;
- have liver disease;
- have or have had cancer or abnormalities of the breast or uterus;
- have overgrowth of the lining of the uterus;
- have undiagnosed or unexpected vaginal bleeding;
- are pregnant or suspect you may be pregnant;
- have a history of heart disease (including heart attack) or stroke;
- have migraine headaches;
- have or have had abnormal increase in blood clotting;
- have partially or completely lost vision due to blood vessel disease of the eye

What the medicinal ingredient is:
Micronized progesterone

What the important nonmedicinal ingredients are:
Non-medicinal ingredients: sunflower oil, gelatin, glycerin, soya lecithin (may contain traces of medium chain triglycerides), titanium dioxide.

What dosage forms it comes in:
Capsules. Each capsule contains 100 mg (milligrams) of micronized progesterone.

WARNINGS AND PRECAUTIONS

Serious Warnings and Precautions

The Women's Health Initiative (WHI) trial assessed the health benefits and risks of oral combined *estrogen plus progestin* therapy and *estrogen-alone* therapy in postmenopausal women.

The WHI trial indicated increased risk of myocardial infarction (heart attack), stroke, invasive breast cancer, pulmonary emboli (blood clots in the lungs) and deep vein thrombosis (blood clots in the large veins) in postmenopausal women receiving combined estrogen plus progestin.

The WHI trial indicated increased risk of stroke and deep vein thrombosis in postmenopausal women with prior hysterectomy (surgical removal of the uterus) receiving estrogen alone.

The Women's Health Initiative Memory Study (WHIMS) estrogen plus progestin ancillary study of the WHI reported an increased risk of probable dementia (madness) in postmenopausal women 65 years of age or older.

Therefore, you should highly consider the following:

- There is an increased risk of developing invasive breast cancer, heart attack, stroke and blood clots in both lungs and large veins with the use of estrogen plus progestin therapy.
- There is an increased risk of stroke and blood clots in the large veins with the use of estrogen-alone therapy.
- Estrogens with or without progestins should not be used for the prevention of heart disease or stroke or dementia.
- Estrogens with or without progestins should be used at the lowest effective dose and for the shortest period of time possible. Regular medical follow-up is advised**.**

Breast Cancer
The results of the WHI trial indicated an increased risk of breast cancer in post-menopausal women taking combined estrogen plus progestin compared to women taking placebo.

The results of the WHI trial indicated no difference in the risk of breast cancer in postmenopausal women with prior hysterectomy taking estrogen-alone compared to women taking placebo.

Estrogens with or without progestins should not be taken by women who have a personal history of breast cancer. In addition, women with a family history of breast cancer or women with a history of breast lumps, breast biopsies or abnormal mammograms (breast x-rays) should consult with their doctor before starting hormone replacement therapy.

Women should have a mammogram before starting HRT and at regular intervals during treatment as recommended by their doctor. Regular breast examinations by a doctor and regular breast self-examinations are recommended for all women. You should review technique for breast self-examination with your doctor.

Ovarian cancer
In some studies, the use of estrogen-alone and estrogen plus progestin therapies for 5 or more years has been associated with an increased risk of ovarian cancer.

Stroke and Heart Disease
The results of the WHI trial indicated an increased risk of stroke and coronary heart disease in post-menopausal women taking combined estrogen plus progestin compared to women taking placebo.

The results of the WHI trial indicated an increased risk of stroke, but no difference in the risk of coronary heart disease in post-menopausal women with prior hysterectomy taking estrogen alone compared to women taking placebo.

Abnormal Blood Clotting
The results of the WHI trial indicated an increased risk of blood clots in the lungs and large veins in post-menopausal women taking combined estrogen plus progestin compared to women taking placebo.

The results of the WHI trial indicated an increased risk of blood clots in the large veins, but no difference in the risk of blood clots in the lungs in post-menopausal women with prior hysterectomy taking estrogen-alone compared to women taking placebo.

The risk of blood clots also increases with age, if you or a family member has had blood clots, if you smoke or if you are severely overweight. The risk of blood clots is also temporarily increased if you are immobilized for long periods of time and following major surgery. You should discuss risk factors for blood clots with your doctor since blood clots can be life-threatening or cause serious disability.

Dementia
The Women's Health Initiative Memory Study (WHIMS) was a substudy of the WHI trial and indicated an increased risk of dementia (loss of memory and intellectual function) in postmenopausal women age 65 and over taking oral combined estrogen plus progestin compared to women taking placebo.

The WHIMS indicated no difference in the risk of dementia in post-menopausal women age 65 and over with prior hysterectomy taking oral estrogen-alone compared to women taking placebo.

BEFORE you use PROMETRIUM® talk to your doctor or pharmacist if you:

- have a history of allergy or intolerance to PROMETRIUM® or any of its ingredients (see What the medicinal ingredient is/ What the important nonmedicinal ingredients are), or are allergic to soya or peanut or to any other substances or medications;
- have a history of liver disease or jaundice (yellowing of

the eyes and/or skin) or itching related to estrogen use or during pregnancy;
- have a personal history of breast disease (including breast lumps) and/or breast biopsies, or a family history of breast cancer);
- have experienced undiagnosed or abnormal vaginal bleeding;
- have a history of uterine fibroids or endometriosis
- have been diagnosed with lupus
- have a history of heart attack, heart disease or stroke;
- have a history of migraine headache;
- have a personal or family history of blood clots or a personal history of active thrombophlebitis (inflammation of the veins);
- have a partial or complete loss of vision due to blood vessel disease of the eye;
- are pregnant or may be pregnant;
- smoke;
- have a history of high blood pressure;
- have a history of kidney disease, epilepsy (seizures) or asthma;
- have a history of bone disease (this includes certain metabolic conditions or cancers that can affect blood levels of calcium and phosphorus) ;
- have been diagnosed with diabetes;
- have been diagnosed with porphyria (a disease of blood pigment);
- have a history of high cholesterol or high triglycerides;
- have a history of depression.
- have had a hysterectomy (surgical removal of the uterus)

PROMETRIUM® may cause some people to feel dizzy or sleepy, 1-4 hours after ingestion of the capsules. Therefore, before you drive or do anything else that requires alertness, make sure you are not experiencing these side effects.

INTERACTIONS WITH THIS MEDICATION

Tell your doctor or pharmacist if you are taking any other medications, including prescription medications, over-the-counter medications, vitamins or herbal products. Some medications (such as certain anti-seizure medications or antibiotics) may affect how PROMETRIUM® Capsules work. PROMETRIUM® Capsules may also affect how your other medicines work.

PROPER USE OF THIS MEDICATION

Usual dose:
Take PROMETRIUM® (micronized progesterone) only as directed by your doctor or pharmacist.

Hormone Replacement Therapy for Menopause

The recommended dose is 2 capsules (200 mg) of PROMETRIUM® per day for the last 14 days of estrogen treatment each cycle or 3 capsules per day (300 mg) for the last 12-14 days of estrogen treatment each cycle. If you are being treated with 2 capsules (200 mg) a day you should take them both at bedtime. If you are being treated with 3 capsules (300 mg) a day, you should split the daily dose in two parts by taking one capsule in the morning and two at bedtime. PROMETRIUM® should be started on the first estrogen cycle. The length of time that you will take PROMETRIUM® will depend of the length of time that you are treated with estrogen. PROMETRIUM® should be taken as long as you take estrogen and you have an intact uterus (have not had surgery to remove the uterus).

A few days after completing a PROMETRIUM® course of 3 capsules daily, the inner lining of the uterus will usually shed. This is accompanied by-vaginal bleeding (resembling a normal monthly period). With a dosage of 2 capsules daily, many women will not have such vaginal bleedings, although the lining of the uterus will also be protected against overgrowth.

Overdose:
When someone accidentally takes too much PROMETRIUM® (micronized progesterone), the following symptoms may arise: nausea, vomiting, sleepiness, dizziness, depressive mood, tiredness, acne and hairiness.

If someone has accidentally taken PROMETRIUM® or has taken several capsules at once, consult a doctor.

In case of overdose, contact your doctor or pharmacist, emergency department of the nearest hospital, a poison control centre immediately

Missed Dose:
If you are being treated with 2 capsules a day (total dose at bedtime) and you forget to take this dose, you should take one capsule the following morning and continue taking the rest of the capsules as prescribed. If you are being treated with 3 capsules a day and you forget to take a morning or evening dose, you should not take the missed dose.

GENERAL THINGS TO REMEMBER:

1. Keep all medication out of the reach of children.
2. This medication has been prescribed only for your current medical condition. Do not use it for other medical problems.
3. Do not allow other people to use your medications and do not use medications meant for other people.
4. Tell any doctor treating you what medications you are taking. Always carry a medical information card stating which medications you are using. This can be very important in case you are involved in an accident.
5. Return unused medications to the pharmacy for safe disposal.
6. Make sure that other people you live with or who look after

you read this information.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Depending on the dosage of PROMETRIUM® (micronized progesterone) and the sensitivity of the patient, the following side effects are possible: genital bleeding or spotting (minor vaginal bleeding) in between the normal periods (mainly during the first two months); irregular menstrual periods; dizziness or vertigo; sleepiness; abdominal discomfort (cramps, pressure, pain); nausea (urge to vomit); fatigue (tiredness); aggravation of migraine headaches, headaches or depressive mood; lightheadedness (feeling faint); breast tenderness/swelling; liver disease.

Side effects observed in women taking progestins in general: a severe allergic reaction which may include hives, itchiness, skin redness, swelling, wheezing, increase heart rate and difficulty breathing; rash with or without itching; rare cases of loss of consciousness; hot flashes; impaired concentration; confusion; swelling; and difficulty with speech.

Other side effects that have been observed with estrogen and progestin combinations in general, but not necessarily with PROMETRIUM® treatment are:

- water retention (bloating, swelling);
- overgrowth of the lining of the uterus;
- gallbladder disorder, impaired liver function, jaundice (yellowing of the eyes or skin);
- menstrual cramps;
- vaginal itching/discharge;
- pain during sexual intercourse;
- pain on urination or difficulty urinating;
- premenstrual syndrome (PMS);
- breast tenderness;
- inflammation of the bladder;
- brown, blotchy spots on exposed skin (pregnancy mask);
- skin rash, tender red lumps or nodules or other skin reactions;
- loss of hair, hairiness;
- acne;
- palpitations (unpleasant sensation of irregular and/or forceful beating of the heart);
- pain, swelling or redness of the calf or leg which may indicate a blood clot;
- chest pain or shortness of breath which may indicate a blood clot;
- increase in blood pressure;
- depression;
- nervousness;
- irritability;
- visual disturbances, intolerance to contact lenses;
- changes in appetite and body weight;
- change in sexual drive;
- pain in the joints and muscles, usually lasting only 3-6 weeks;
- headache.

During your first 2-4 months of HRT, you may experience minor unscheduled vaginal bleeding (at times other than when you would expect a normal period). This is a normal response of your body as it adjusts to the return of estrogen and progesterone to the levels that were seen before menopause. Should unscheduled vaginal bleeding persist, you should consult your doctor.

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Frequency	Symptom/effect	Talk with your doctor or pharmacist		Stop taking drug and call your doctor or pharmacist
		Only if severe	In all cases	
At any frequency	Abdominal pain, nausea or vomiting		√	
	Breast lump		√	
	Crushing chest pain or chest heaviness			√
	Pain or swelling in the leg			√
	Persistent sad mood			√
	Sharp pain in the chest, coughing blood or sudden shortness of breath			√
	Sudden partial or complete loss of vision			√
	Sudden severe headache or worsening of headache, vomiting, dizziness, fainting, disturbance of vision or speech or weakness or numbness in an arm or leg (any of these, alone or in combination)			√
	Unexpected vaginal bleeding		√	
	Yellowing of the skin or eyes (jaundice)			√

This is not a complete list of side effects. For any unexpected effects while taking PROMETRIUM, contact your doctor or pharmacist.

HOW TO STORE IT

The capsules should be stored at controlled room temperature between 15°C and 30°C (59°F and 86°F). The date the capsules should be used by is printed on the strip after the term "Exp." (expiry date). Protect from light.

REPORTING SIDE EFFECTS

You can help improve the safe use of health products for Canadians by reporting serious and unexpected side effects to Health Canada. Your report may help to identify new side effects and change the product safety information.

3 ways to report:

- Online at MedEffect;
- By calling 1-866-234-2345 (toll-free);
- By completing a Consumer Side Effect Reporting Form and sending it by:
  - Fax to 1-866-678-6789 (toll-free), or
  - Mail to: Canada Vigilance Program
    Health Canada, Postal Locator 0701E
    Ottawa, ON
    K1A 0K9

  Postage paid labels and the Consumer Side Effect Reporting Form are available at MedEffect.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice. »

MORE INFORMATION

If you want more information about PROMETRIUM®:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Consumer Information by visiting the Health Canada website or Merck Canada web site www.merck.ca or by calling Merck Canada at 1-800-567-2594

To report an adverse event related to PROMETRIUM®, please contact 1-800-567-2594.

This leaflet was prepared by Merck Canada Inc.

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