PART III: CONSUMER INFORMATION

PR PROVERA*
(medroxyprogesterone acetate)

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

ABOUT THIS MEDICATION

What the medication is used for:

- Hormonal Replacement Therapy for Menopause – PROVERA is used for women with intact uteri who are also receiving estrogen therapy.
- To Treat Menstrual Disorders due to Hormonal Imbalance - In non-pregnant women, PROVERA helps to balance the effect of estrogen.

- To Treat Cancer:
  - To treat and relieve symptoms associated with endometrial cancer.
  - To treat and relieve symptoms of breast cancer in postmenopausal women.

PROVERA should be used only under the supervision of a doctor, with regular follow-up at least once a year to identify the 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.

Progestin, when used with estrogen therapy, have important benefits but also some risks. You should carefully discuss the risks and benefits of hormone replacement therapy (HRT) with your doctor. If you use progestin with estrogen therapy, check with your doctor to be sure you are using the lowest possible dose that works, and that you don't use them longer than necessary. How long you need to use HRT will depend on the reason for use. You should regularly talk with your doctor about whether you still need treatment with HRT.

If you have any questions about this medication or your condition, please ask your doctor or pharmacist.

What it does:

PROVERA (medroxyprogesterone acetate) is a hormone replacement therapy (HRT) that contains a manufactured progesterone hormone, progestin, that is similar to the progesterone produced by a woman's ovaries.

When given with an appropriate dose of estrogen hormone, PROVERA significantly reduces the risk of developing endometrial hyperplasia (overgrowth of the uterus lining) and the risk of cancer of the uterus. Seven (7) days after stopping PROVERA treatment, you should have withdrawal bleeding. If bleeding occurs during the PROVERA treatment, talk to your doctor, as the dose may need to be modified.

Progesterone therapy regulates bleeding patterns. When given to non-pregnant women to treat menstrual disorders, the endometrium (inner lining of the uterus) does not grow as much and bleeding decreases. This is because PROVERA helps to balance the effect of estrogen. You will know that PROVERA is effective if it induces a period (any bleeding more than light spotting) within 2 weeks after PROVERA is given. This bleeding will usually occur 2-7 days after the PROVERA is finished.

For Oncology:
When used to treat cancer, PROVERA is thought to work two-ways: it decreases hormone release and it prevents the cancer cells from multiplying by balancing out high levels of estrogen. The response to hormonal therapy for endometrial or breast cancer may not be evident until 8 to 10 weeks of therapy.

When it should not be used:

You should not take PROVERA if you have any of the following conditions:

- In the presence of liver disease;
- If you have had or have cancer of the breast or uterus, unless PROVERA is being used to treat and relieve the symptoms associated with these cancers;
- If you have abnormal vaginal bleeding;
- If you are pregnant;
- If you have had or have any blood circulation problems, such as blood clots, stroke, blindness or migraine headaches;
- If you have had a stroke or heart attack;
- If you have had an unusual allergic response to progestin or to any of the ingredients in the tablet.

Do not take PROVERA for conditions for which it was not prescribed. Do not give PROVERA to other people, even if they have the same symptoms you have. It may harm them.

What the medicinal ingredient is:

Medroxyprogesterone acetate

What the nonmedicinal ingredients are:

PROVERA tablets also contain calcium stearate, corn starch, lactose monohydrate, mineral oil, sucrose, talc. The 2.5 mg tablet contains FD&C Yellow No. 6 and the 5 mg tablet contains FD&C Blue No.2 aluminum lake.

What dosage forms it comes in:

PROVERA tablets are available as:

- 2.5 mg circular, orange tablets embossed with "U 64" on one side and scored on the other.
- 5 mg circular, blue tablets embossed with "U 286" on both sides of a break score and on the other surface with "U".
- 10 mg circular, white tablets embossed with "Upjohn 50" on one side and scored on the other.

WARNINGS AND PRECAUTIONS

Serious Warnings and Precautions

The Women's Health Initiative (WHI) trial is a large clinical study that assessed the benefits and risks of oral combined *estrogen plus progestin* therapy and oral *estrogen-alone* therapy compared with placebo (a pill with no active ingredients) in postmenopausal women.

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

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

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.
- 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 HRT.

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.

Overgrowth of the lining of the uterus and cancer of the uterus

The use of *estrogen-alone* therapy by post menopausal women who still have a uterus increases the risk of developing endometrial hyperplasia (overgrowth of the lining of the uterus), which increases the risk of endometrial cancer (cancer of the lining of the uterus).

The purpose of adding a progestin medication to estrogen therapy is to reduce the risk of endometrial hyperplasia.

You should discuss progestin therapy and risk factors for endometrial hyperplasia and endometrial carcinoma with your doctor. You should also report any unexpected or unusual vaginal bleeding to your doctor.

If you have had your uterus removed, you are not at risk of developing endometrial hyperplasia or endometrial carcinoma. Progestin therapy is therefore not generally required in women who have had a hysterectomy.

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.

Heart Disease and Stroke

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.

Gallbladder Disease

The use of estrogens by postmenopausal women has been associated with an increased risk of gallbladder disease requiring surgery.

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 PROVERA talk to your doctor or pharmacist if:

- have a history of allergy or intolerance to any medications or other substances
- have a personal history of breast disease (including breast lumps) and/or breast biopsies, or a family history of breast cancer
- have experienced any unusual or undiagnosed vaginal bleeding
- have a history of uterine fibroids or endometriosis
- have a history of liver disease, jaundice (yellowing of the eyes and/or skin) or itching related to estrogen use or during pregnancy
- have a history of migraine headache
- have a history of high blood pressure
- have a personal or family history of blood clots, or a personal history of heart disease or stroke
- have a history of kidney disease, asthma or epilepsy (seizures)
- 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
- are pregnant or may be pregnant
- have had a hysterectomy (surgical removal of the uterus)
- smoke

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.

Drugs that may interact with PROVERA include:

- Preparations inducing liver enzymes (eg. barbiturates, hydantoins, carbamazepine, meprobamates, phenylbutazone or rifampin);
- Aminoglutethimide;
- Some herbal (eg. St. John's wort) and natural products which are bought without a prescription.

PROPER USE OF THIS MEDICATION

PROVERA should be taken by mouth.

PROVERA can be taken with or without food.

Usual dose:

1. **Hormonal Replacement Therapy for Menopause**
   The recommended dose for women is 5 to 10 mg daily for 12 to 14 days.

2. **Functional Menstrual Disorders due to Hormonal Imbalance**
   (a) *Secondary amenorrhea (absence of menstrual period)*: After ruling out pregnancy, PROVERA, may be administered in doses ranging from 5 to 10 mg daily for 12 to 14 days every month.
   (b) *Dysfunctional uterine bleeding:* PROVERA may be given in doses ranging from 5 to 10 mg daily for 10 to 14 days, beginning on the 12th to 16th day of the cycle. This regimen should be repeated for 2 subsequent cycles or longer if necessary.

3. **Endometrial Cancer**
   The recommended dose is 200 to 400 mg daily.

4. **Breast Cancer**
   The recommended dose is 400 mg daily, given in divided doses.

   It is important that you take PROVERA regularly at the same time each day.

Overdose:

Symptoms: Overdosage may result in a period of amenorrhea (absence or cessation of menstrual period) and may be followed by irregular menses for several cycles.

For management of a suspected drug overdose, contact your regional Poison Control Centre

Missed Dose:
Do not take a double dose to make up for a forgotten tablet. If you miss a dose, take it as soon as you can if it is within 12 hours of the missed dose. If it is over 12 hours since your missed dose, skip the missed dose and go back to your usual dosing times

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

The following side effects have been reported with the use of PROVERA:

- Breast tenderness;
- Breast milk secretion;
- Breakthrough bleeding;
- Spotting (minor vaginal bleeding);
- Irregular menstrual periods;
- Amenorrhea (absence of menstrual periods);
- Vaginal secretions;
- Headaches;
- Nervousness;
- Dizziness;
- Insomnia, sleepiness, fatigue;
- Premenstrual syndrome-like symptoms;
- Itching, hives, skin rash;
- Acne;
- Hair loss, hair growth;
- Abdominal discomfort; nausea; bloating;
- Fever;
- Increase in weight;
- Swelling;
- Moon shaped face.

If you experience any of these side effects, contact your doctor or pharmacist.

The side effects listed in the table below have been observed with estrogen/progestin combination in general, but not necessarily with PROVERA.

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

Frequency	Symptom / possible side effect	Talk with your doctor or pharmacist		Stop taking drug and call your doctor or pharmacist
		Only if severe	In all cases	
Not known	Persistent sad mood			√
	Abdominal pain, nausea or vomiting		√	
	Pain or swelling in the leg /inflamed vein			√
	Breast lump		√	
	Sharp pain in the chest, coughing blood or sudden shortness of breath			√
	Sudden severe headache or worsening of headache, vomiting, dizziness, fainting, disturbance of vision or speech or weakness or numbness in an arm or leg			√
	Sudden partial or complete loss of vision			√
	Unexpected vaginal bleeding		√	
	Yellowing of the skin or eyes (jaundice)			√
	Crushing chest pain or chest heaviness			√

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

HOW TO STORE IT

PROVERA should be stored at controlled room temperature, 15-30°C. Keep out of the reach of children.

REPORTING SUSPECTED SIDE EFFECTS

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

- **Report online at www.healthcanada.gc.ca/medeffect**
- **Call toll-free at 1-866-234-2345**
- **Complete a Canada Vigilance Reporting Form and:**
  - **Fax toll-free to 1-866-678-6789, or**
  - **Mail to: Canada Vigilance Program**
    Health Canada
    Postal Locator 0701C
    Ottawa, ON K1A 0K9

Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect™ Canada Web site at www.healthcanada.gc.ca/medeffect.

NOTE: **Should you require information related to the management of side effects, contact your health professional. The Canada Vigilance Program does not provide medical advice.**

MORE INFORMATION

This document plus the full product monograph, prepared for health professionals, may be obtained at: http://www.pfizer.ca or by contacting the sponsor, Pfizer Canada Inc. at: 1-800-463-6001.

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