INFORMATION FOR THE PATIENT

This leaflet describes the uses of estrogens and progestins, precautions to take when using these hormones and how to use CLIMARA PRO. Please read it carefully. If you want to know more or have any questions, please ask your doctor or pharmacist.

WARNING

The Women's Health Initiative (WHI) study results indicated increased risk of myocardial infarction (heart attack), stroke, invasive breast cancer, pulmonary emboli (blood clots in the lungs) and deep venous thrombosis (blood clots in the leg veins) in postmenopausal women receiving treatment with conjugated equine estrogens (an estrogen medication) combined with medroxyprogesterone acetate (a progestin medication) compared to women receiving placebo (sugar tablets).

Other combinations of estrogens and progestins were not studied. In the absence of comparable data, these risks should be assumed to be similar.

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 legs and lungs, with treatment.
- Estrogens with or without progestins should not be prescribed for prevention of heart disease or stroke.
- Estrogens with or without progestins should be prescribed at the **lowest effective dose** and for the **shortest period of time** possible.

INTRODUCTION: What is CLIMARA PRO?

The CLIMARA PRO transdermal system (patch) is a hormone replacement therapy (HRT) that contains the hormone estrogen (estradiol), the same hormone that is produced naturally in the body, as well as a progestin, levonorgestrel. A CLIMARA PRO patch is worn continuously for one week on the abdomen or buttocks, and provides continuous, controlled delivery of 45 µg estradiol and 15 µg levonorgestrel per day, through the skin into the bloodstream. A new patch should be applied once a week during each 28-day cycle.

Your doctor has prescribed CLIMARA PRO for you after a careful review of your medical needs. Use it only as directed and do not give it to anyone else. CLIMARA PRO must only be used under the supervision of your doctor, with regular check-ups at least once a year, to identify possible adverse events associated with treatment.

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

INDICATIONS

CLIMARA PRO is approved to provide relief from the symptoms of menopause.

Uses of Estrogens

When a woman's menstrual periods cease (menopause) around the age of 50, the ovaries stop producing estrogens, the main female hormones. Sometimes the ovaries are removed by an operation causing "surgical menopause". When the amount of estrogen produced by the body begins to decrease, some women develop very uncomfortable symptoms, such as feelings of warmth in the face, neck, and chest, or sudden intense episodes of heat and sweating ("hot flushes"). Hot flushes can cause frequent awakening at night, with sleep disturbance leading to fatigue, irritability, and depression. The use of estrogen replacement can stop or greatly reduce the occurrence of menopausal flushes.

As a result of estrogen deficiency, changes also occur in and around the vagina (causing itching, burning, dryness, painful intercourse) and urethra (causing difficulty or burning on urination, and frequent urination). These changes may improve with estrogen therapy.

Uses of Progestins

Progestins used in hormone replacement therapy have similar effects to the female sex hormone progesterone. During child bearing years, progesterone is responsible for regulation of the menstrual cycle. The estradiol delivered by CLIMARA PRO not only relieves your menopausal symptoms, but, like estrogens produced by your body, may also stimulate growth of the inner lining of the uterus, the endometrium. In menopausal and postmenopausal women with an intact uterus, stimulation of growth of the endometrium may result in irregular bleeding. In some cases this may progress into a disorder of the uterus known as endometrial hyperplasia (overgrowth of the lining of the uterus). Endometrial hyperplasia increases the risk of endometrial cancer (cancer of the lining of the uterus). The risk of endometrial hyperplasia is reduced if a progestin medication, such as levonorgestrel, is given together with estrogen replacement therapy.

If you have had a hysterectomy (surgical removal of the uterus), endometrial

hyperplasia cannot occur and administration of a progestin is not necessary. Therefore, CLIMARA PRO **should not** be used by women who have had a hysterectomy.

RESTRICTIONS ON USE: WHO SHOULDN'T USE CLIMARA PRO

You **should not** use CLIMARA PRO if you:

- Have active liver disease
- Have a personal history of breast cancer or endometrial cancer (cancer of the lining of the uterus).
- Have been diagnosed with endometrial hyperplasia (overgrowth of the lining of the uterus).
- Have experienced undiagnosed or abnormal genital bleeding.
- Have a history of heart attack, heart disease or stroke.
- Experience migraine headaches.

- Have a personal history of blood clots or active thrombophlebitis (inflammation of the veins).
- Have had partial or complete loss of vision due to blood vessel disease of the eye.
- Are pregnant or think you may be pregnant. (Since pregnancy may be possible early in menopause while you are still having spontaneous periods, the use of non-hormonal birth control should be discussed with your doctor at this time. If you take estrogen during pregnancy, there is a small risk of your unborn child having birth defects.
- Are breast feeding.
- Have had a hysterectomy (surgical removal of the uterus).
- Have had an allergic or unusual reaction to estrogen, progestin or any component of CLIMARA PRO (see the **PHARMACEUTICAL INFORMATION** section of this leaflet).

WARNINGS AND PRECAUTIONS

See the **Boxed Warnings** at the front page.

Endometrial Hyperplasia (overgrowth of the lining of the uterus) and Endometrial Carcinoma (cancer of the lining of the uterus)

CLIMARA PRO contains an estrogen and a progestin. If you have not had a hysterectomy (surgical removal of the uterus), estrogens may stimulate growth of the endometrium (the lining of the uterus). In some cases this can progress into a disorder of the uterus known as endometrial hyperplasia (overgrowth of the lining of the uterus). Endometrial hyperplasia increases the risk of development of endometrial carcinoma (cancer of the lining of the uterus). You should discuss other risk factors for the development of endometrial cancer with your doctor.

The risk of endometrial hyperplasia and endometrial carcinoma is reduced if a progestin medication is given together with estrogen replacement therapy.

If you have had your uterus surgically removed, you are not at risk of developing endometrial hyperplasia and administration of a progestin is not necessary. Therefore, CLIMARA PRO **should not** be used by women who have had a hysterectomy.

Cancer of the breast

The long-term use (more than 4 years) of combined estrogen and progestin therapy by postmenopausal women has been associated with an increased risk of invasive breast cancer.

For this reason, estrogens 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 personal history of breast lumps, breast biopsies or abnormal mammograms (breast x-rays) should consult with their doctor before starting hormone replacement therapy (HRT). You should discuss risk factors for the development of breast cancer with your doctor.

Women should have a mammogram before starting HRT and at regular intervals during treatment as recommended by their treating physician.

Regular breast examinations by a physician and regular breast self-examinations are recommended for all women.

Cardiovascular disease (heart disease and stroke)

The use of combined estrogen and progestin therapy by postmenopausal women has been associated with an increased risk of heart attack and stroke. You should discuss risk factors for the development of heart disease and stroke with your doctor.

Venous thromboembolism (blood clots in the veins)

The use of combined estrogen and progestin therapy by postmenopausal women has been associated with an increased risk of blood clots in the legs and lungs. This risk 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 with major surgery. You should discuss risk factors for the development of blood clots with your doctor.

Your doctor may recommend that you temporarily discontinue taking hormone replacement therapy in advance of expected hospitalizations or surgery.

Gallbladder disease

Women who use estrogens after menopause are more likely to develop gallbladder disease than women who do not use estrogens.

Dementia

Current studies indicate that the use of combined estrogen and progestin in women aged 65 and over may increase the risk of developing probable dementia (loss of memory and intellectual function).

Precautions

Certain medical conditions may be aggravated by estrogens or progestins. Therefore, these hormones should either not be used at all or should be used with caution under these conditions.

To help your doctor decide whether you should use CLIMARA PRO and what precautions should be taken during use, tell your doctor:

- what other prescription and nonprescription medicines, if any, you are taking (including herbal products, such as St. John's wort). There are some medicines which may interfere with the effects of CLIMARA PRO (e.g., phenytoin, carbamazepine, rifampicin), and CLIMARA PRO may interfere with the effects of other medicines (e.g., medications for thinning the blood, medications for diabetes, medications for high blood pressure).
- about any allergies or sensitivities to medicines or any other substances you may have.
- if you are undergoing surgery or need long bed rest.
- if any of the following conditions apply to you:
  - have a history of liver disease;
  - have a history of jaundice (yellowing of the eyes and/or skin) or itching related to estrogen use or during pregnancy;
  - have a personal or family history of known or suspected breast cancer or a personal history of endometrial cancer (cancer of the lining of the uterus);
  - have a personal history of breast disease (including breast lumps) and/or breast biopsies;
  - have a history of endometrial hyperplasia (overgrowth of the lining of the uterus);

- have been diagnosed with high prolactin levels or prolactinoma;
- have experienced undiagnosed or abnormal vaginal bleeding;
- have a history of heart attack, heart disease or stroke;
- experience migraine headaches;
- have a personal or family history of blood clots or a personal history of active thrombophlebitis (inflammation of veins);
- have had partial or complete loss of vision due to blood vessel disease of the eye;
- are pregnant or may be pregnant;
- are breast feeding;
- have had a hysterectomy (surgical removal of the uterus);
- have a history of allergy or intolerance to any medications or other substances;
- smoke;
- have a history of kidney disease, asthma or epilepsy (seizures);
- have a history of bone disease (this includes metabolic conditions or cancers that can affect blood levels of calcium and phosphorus);
- have a history of high blood pressure;
- have been diagnosed with diabetes;
- have been diagnosed with porphyria (an abnormality of metabolism that can cause light sensitivity, abdominal pain and mental confusion)
- have a history of high cholesterol or high triglycerides (a fat-like substance in the blood);
- have a history of uterine fibroids (non-cancerous growths of the uterus) or endometriosis (growth outside of the uterus made up of tissues that line the uterus);
- have a history of depression.
- suffer from episodes of swelling in body parts such as hands, feet, face, airway passages that are caused by a defect in the gene that controls a blood protein called CI-inhibitor (hereditary angioedema)

Monitoring Your Health While on Hormone Replacement Therapy

See your doctor regularly. While you are taking CLIMARA PRO, it is important to visit your doctor at least once a year for a physical examination. Your visit may include a blood pressure check, a breast exam and a Pap smear and pelvic exam. Your doctor may also recommend some blood tests. A mammogram (breast x-ray) is suggested before starting treatment and at regular intervals as suggested by your doctor.

Regular breast examinations by a physician and regular breast self-examinations are recommended for all women. You should review technique for breast self- examination with your doctor.

Unexpected or undiagnosed vaginal bleeding should be investigated by your doctor.

ADVERSE EFFECTS

See also the **WARNINGS AND PRECAUTIONS** section of this leaflet.

The following side effects have been reported in women taking estrogen-progestin combinations (such as CLIMARA PRO). Check with your doctor if you develop any of these symptoms:

- retention of fluid

- migraine headaches
- localized darkening of the skin
- breast tenderness and/or excessive vaginal secretions (may be a sign that too much estrogen is taken)
- persistent upper abdominal pain, nausea, vomiting, tender abdomen (may be signs of gallbladder disease)
- lower abdominal pain or swelling, painful and/or heavy periods (may be signs of growth of fibroids in the uterus)
- yellowing of the eyes or skin (may be signs of jaundice)
- upper abdominal pain or swelling (may be signs of liver tumors)
- mood swings
- changes in body weight

Estrogens produced outside the body may cause or worsen symptoms of swelling in body parts such as hands, feet, face, and airway passages.

In addition, CLIMARA PRO may produce some redness or irritation under or around the patch in some women (see **Helpful Hints**).

Check with your doctor as soon as possible if any of the following occur:

- irregular or unusual vaginal bleeding
- changes in speech
- dizziness and faintness
- vomiting
- intolerable breast tenderness
- breast enlargement or lumps
- severe headaches
- changes in vision
- persistent or severe skin irritation
- fluid retention or bloating persisting for more than 6 weeks

Check with your doctor immediately if you experience:

- trouble breathing or tightness of the chest
- severe pain in one or both legs or numbness suddenly affecting one side or one part of the body
- sudden change in vision
- first migraine headache
- skin redness, warmth, swelling, tenderness, pain or hardening of tissue around a vein
- pain or heaviness in the legs or chest
- sudden shortness of breath
- coughing of blood
- rapid pulse or dizziness
- any other unusual symptom

These are not all of the possible side effects of estrogen/progestin therapy. If you experience any side effects or for more information, contact your doctor or your pharmacist.

HOW TO USE CLIMARA PRO

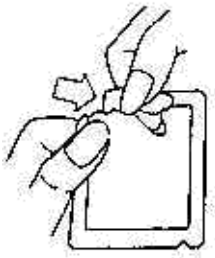
How CLIMARA PRO Works

The CLIMARA PRO patch contains both estradiol and levonorgestrel. When applied to the skin as directed below, CLIMARA PRO continually releases small, controlled amounts of estradiol and levonorgestrel, which pass through the skin into the bloodstream. Estradiol provides relief from menopausal symptoms and levonorgestrel provides important protection for your uterus (See **Uses of Progestins**).

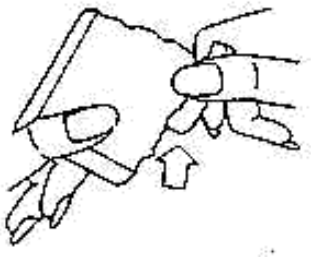
Each CLIMARA PRO patch is individually sealed in a protective pouch. A protective liner covers the adhesive side of the patch - the side that will be placed against your skin. This liner must be removed before applying the patch. See below for instructions on how to apply CLIMARA PRO.

How to Apply CLIMARA PRO

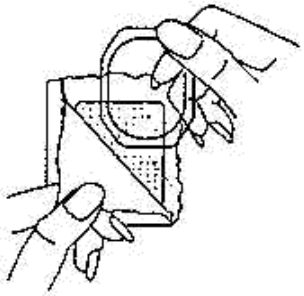
Never cut the pouch with scissors – you might damage the patch inside. To open the pouch, hold it vertically with the CLIMARA PRO name facing you. Tear the pouch at the notch provided at the top of the left-hand corner, tearing from left to right.



Next, open the right side of the pouch using the notch at the bottom of the right-hand corner and tear from bottom to top.

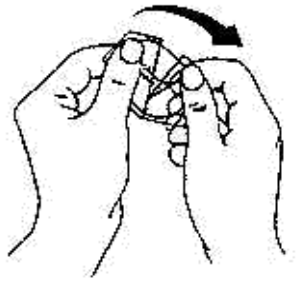


Carefully remove the patch.

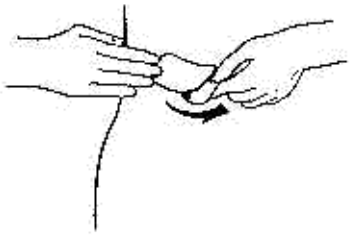


A protective plastic backing covers the adhesive side of the patch and must be removed before applying it. The patch itself is oval and translucent.

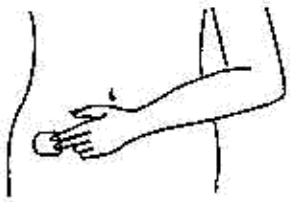
Peel off one side of the protective backing. Try to avoid touching the adhesive side of the patch.



Using the other half of the backing as a handle, apply the sticky side of the patch to the skin. Peel away the other side of the backing and press the entire patch firmly to the skin (see **Where to Apply CLIMARA PRO**, below). Discard the protective backing.

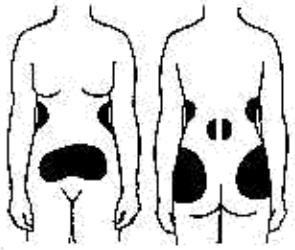


Apply firm pressure around the edges for about 10 seconds to make sure there are no air bubbles under the patch. If the patch lifts, pressure should be applied to maintain adhesion.



Where to Apply CLIMARA PRO

Apply the adhesive side of the patch to a clean dry area of the skin on the sides, lower back or abdomen of your body or buttocks. **Do not apply CLIMARA PRO to your breasts due to potentially harmful effects on the breast tissue.** Avoid the waistline, since tight clothing may rub and remove the patch. Application to areas where sitting would dislodge the patch should also be avoided. The sites of application in the chosen body area (for example, buttocks) must be rotated, with an interval of at least 1 week allowed between applications to a particular site. The area selected should not be oily, damaged, or irritated. Apply the patch immediately after opening the pouch and removing the protective liner (see **How to Apply CLIMARA PRO**, above). Press the patch firmly in place with the fingers for about 10 seconds, making sure there is good contact, especially around the edges. If the patch lifts, pressure should be applied to maintain adhesion.



CLIMARA PRO should be worn continuously for one week. You may wish to experiment with different locations when applying a new patch, to find ones that are most comfortable for you and where clothing will not rub on the patch.

When to Apply CLIMARA PRO

The CLIMARA PRO patch should be changed once weekly. When changing the patch, remove the used CLIMARA PRO patch. Carefully fold it in half so that it sticks to itself, because used patches still contain active hormones, and throw it away, safely out of the reach of children or pets. Any adhesive that might remain on your skin can be easily rubbed off. Then place the new CLIMARA PRO patch on a different skin site. (The same skin site should not be used again for at least 1 week after removal of the patch).

Contact with water when you are bathing, swimming or showering should not affect the patch. In the unlikely event that a patch should fall off, you may reapply the same patch to a new area of skin and continue with your regular schedule. Make sure that there is good contact, especially around the edges. If the patch will not stick completely to your skin, then apply a new patch to a new area of skin for the remainder of the 7-day dosing interval. **Do not apply two patches at the same time.**

Once in place, the patch should not be exposed to the sun for prolonged periods of time.

How CLIMARA PRO is supplied

CLIMARA PRO is supplied in boxes containing 4 patches.

Helpful Hints

What to do if the patch falls off. Should a patch fall off in a very hot bath or shower, shake the water off the patch. Dry your skin completely and try to reapply the patch to a new site and continue your regular schedule. If it still does not stick, then apply a **new** patch to a new site and continue with your regular schedule.

In addition, there are some other causes for the patch failing to stick. If you are having patches fall off regularly, this could be happening as a result of:

- using any type of bath oil
- using soaps with a high cream content
- using skin moisturizers before applying the patch

Patch adhesion may be improved if you avoid using these products, and by cleansing the site of application with rubbing alcohol before you apply the patch.

What to do if your skin becomes red or irritated under or around the patch.

As with any product that covers the skin for a period of time (such as bandages), the CLIMARA PRO patch can produce some skin irritation in some women. This varies according to the sensitivity of each woman.

Usually this redness does not pose any health concern to you, but to reduce this problem, there are some things that you may do:

- Choose the buttocks as the site of application
- Change the site of application of the CLIMARA PRO patch every time a new patch is applied, usually once weekly.

If redness and/or itching continues, you should consult your doctor.

Always Remember

Your doctor has prescribed CLIMARA PRO for you after a careful review of your medical needs. Use it only as directed and do not give it to anyone else. Your doctor should re-examine you at least once a year.

If you have any questions, contact your doctor or pharmacist.

SYMPTOMS AND TREATMENT OF OVERDOSAGE

Symptoms: Overdosage with estrogen or progestin containing products may cause nausea, breast discomfort, fluid retention, bloating, vaginal bleeding, depressed mood, tiredness, acne and hirsutism (excessive hair growth).

Treatment: If you think you have taken an overdose of CLIMARA PRO, remove the patch(es) immediately and call your doctor, hospital, or poison control centre.

PHARMACEUTICAL INFORMATION

The medicinal ingredients in CLIMARA PRO are estradiol and levonorgestrel. CLIMARA PRO also contains the non-medicinal ingredients acrylate copolymer adhesive and polyvinylpyrrolidone/vinyl acetate copolymer.

STORAGE

CLIMARA PRO patches should be stored at room temperature, between 15°C and 30°C. Do not refrigerate or freeze. Apply CLIMARA PRO immediately upon removal from the protective pouch. **Do not store the patches out of the pouch.**

CLIMARA PRO should be kept out of the reach of children and pets before and after use.

REPORTING SUSPECTED 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 (http://hc-sc.gc.ca/dhp-mps/medeff/index-eng.php);
- 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 (http://hc-sc.gc.ca/dhp-mps/medeff/index-eng.php).

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

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