PART III: CONSUMER INFORMATION

Pr CLIMARA ® 25
PrCLIMARA® 50
PrCLIMARA® 75
PrCLIMARA® 100

estradiol hemihydrate transdermal system

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

ABOUT THIS MEDICATION

What the medication is used for:

CLIMARA is approved for use in the following situations:

- To provide relief from the symptoms of menopause

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 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 can occur in and around the vagina (causing itching, burning, dryness, painful intercourse) and urethra (causing difficulty or burning during urination and frequent voiding). These changes may improve with estrogen therapy.

CLIMARA 50, CLIMARA 75 and CLIMARA 100 are approved for use in the following situations:

- To help prevent you from developing osteoporosis (thin weak bones)

After menopause, all women start to lose calcium from their bones at an accelerated rate due to a decrease in the amount of estrogen produced by the body. In time, this may cause a thinning of the bones called osteoporosis which makes them weaker and more likely to break, often leading to fractures of the vertebrae, hip and wrist bones. Taking estrogens after menopause may slow down bone loss and may prevent bones from breaking.

CLIMARA is to be considered in light of other available therapies for the prevention of postmenopausal osteoporosis. Discuss adequate diet, calcium and vitamin D intake, cessation of smoking as well as regular physical weight bearing exercise with your doctor or pharmacist in addition to the administration of CLIMARA.

Those women who are likely to develop osteoporosis include those with a strong family history of osteoporosis or bone fractures in older ages, and those who are white, thin, smoke cigarettes, and do not exercise.

Women who have an early menopause or undergo removal of their ovaries at an early age are at greater risk of developing osteoporosis at an earlier age.

In women with intact uteri, CLIMARA should always be taken with a progestin. If your uterus has been surgically removed, endometrial hyperplasia cannot occur and cyclical administration of a progestin is not necessary.

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

Uses of Progestins:

The estradiol delivered by CLIMARA may not only relieve 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 intact uteri, 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), which increases the risk of endometrial cancer (cancer of the lining of the uterus). The risk of endometrial hyperplasia is reduced if a progestin medication is given regularly for a certain number of days with your estrogen replacement therapy.

CLIMARA 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:

CLIMARA is a medicated patch that contains the hormone estrogen (estradiol), the same hormone that is produced naturally in the body. When you place this patch on your skin, the hormone is transferred to your body through your skin.

When it should not be used:

- You should not take CLIMARA if you:
- are pregnant or if you are breastfeeding
- have active liver disease, or have or have ever had a liver tumour (benign or malignant)
- have a personal history of certain types of cancer, such as endometrial cancer (cancer of the lining of the uterus). If you have or had cancer, talk with your doctor about whether you should take CLIMARA
- have known, suspected or past history of breast cancer. If you have or had cancer, talk with your doctor about whether you should take CLIMARA
- 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
- have a personal history of blood clots or active thrombophlebitis (inflammation of the veins)
- are at high risk of having a blood clot including if you were born with certain blood clotting disorders
- have had partial or complete loss of vision due to blood vessel disease of the eye
- have had an allergic or unusual reaction to estrogen or any component of CLIMARA

What the medicinal ingredient is:

estradiol hemihydrate

What the nonmedicinal ingredients are:

acrylate copolymer (consisting of isooctyl acrylate, acrylamide, vinyl acetate copolymer), ethyl oleate, glyceryl monolaurate, isopropyl myristate

What dosage forms it comes in:

The CLIMARA patch is available in four sizes: CLIMARA 25 (containing 2.0 mg of estradiol), CLIMARA 50 (containing 3.8 mg of estradiol), CLIMARA 75 (containing 5.7 mg of estradiol) and CLIMARA 100 (containing 7.6 mg of estradiol).

Each box of CLIMARA contains 4 patches.

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 post-menopausal women with prior hysterectomy taking estrogen-alone compared to women taking placebo.

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 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. The use of HRT may make it more difficult to detect breast cancer by mammography, in some cases.

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.

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).

If you still have your uterus you should take a progestin medication (another hormone drug) regularly for a certain number of days 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.

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 post-menopausal 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.

Skin Sensitivity

Contact sensitization (extreme sensitivity of the skin) has been known to occur with the use of topical applications (medications which are applied to the skin). Although it is extremely rare, patients who develop contact sensitization to any component of the patch may have a severe hypersensitivity reaction (i.e. allergic reaction) with continued use of the patch.

Tumours on the Liver

Benign tumours on the liver have been associated with the use of combined estrogen and progestin oral contraceptives. Although benign and rare, these tumours may rupture and cause death from bleeding in the

abdominal cavity. Such tumours have not yet been reported in association with other estrogen or progestin preparations, but they should be considered if abdominal pain and tenderness occurs, or if there is a large abdominal mass, or if sudden and significant drop in blood pressure occurs as a result of the bleeding. Liver cancer has also been reported in women taking estrogen-containing oral contraceptives, however, it is not known if this occurred as a result of taking these drugs.

BEFORE you use CLIMARA talk to your doctor or pharmacist if you:

- 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 or have had chloasma (yellow-brown patches on the skin);
- have inherited deafness (otosclerosis)
- have systemic lupus erythematosus (SLE; a chronic inflammatory disease)
- have or have had chorea minor (illness with unusual movements)
- have been told that you have a condition called hereditary angioedema or if you have episodes of rapid swelling of hands, feet, face, lips, eyes, tongue, throat (airway blockage), or digestive tract
- 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
- are undergoing surgery or need long bed rest
- 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 been diagnosed with high prolactin levels or prolactinoma
- have a history of high cholesterol or high triglycerides
- are pregnant or may be pregnant
- are breastfeeding
- have had a hysterectomy (surgical removal of the uterus)
- smoke
- have a history of depression

Driving or Using Machines

The effects of CLIMARA on the ability to drive or to use machines have not been studied.

INTERACTIONS WITH THIS MEDICATION

Tell your doctor if you are taking any other medications, including prescription and non-prescription medications, over-the-counter medications, vitamins or herbal products. There are some medicines which may interfere with the effects of CLIMARA and CLIMARA may interfere with the effects of other medicines.

Drugs that may interact with CLIMARA include:

- anticoagulants, antidiabetic agents
- drugs used for the treatment of certain heart diseases or high blood pressure (eg, diltiazem, verapamil)
- drugs used for the treatment of HIV infections and Hepatitis C Virus infections (e.g., nelfinavir, ritonavir, ritonavir-boosted protease inhibitors, boceprevir, telaprevir, nevirapine)
- barbiturates, carbamazepine, meprobamate, phenylbutazone, primidone, phenytoin, oxcarbazepine, topiramate, felbamate or rifampicin
- antibiotics (eg, erythromycin, clarithromycin, penicillin, tetracycline)
- antifungals (eg, griseofulvin, fluconazole, itraconazole, ketoconazole, voriconazole)
- antivirals (ritonavir)

Alcohol, grapefruit juice and St. John’s wort may also interact with CLIMARA.

PROPER USE OF THIS MEDICATION

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.

Usual dose:

The CLIMARA patch contains estradiol. When applied to the skin as directed below, CLIMARA releases estradiol which passes through the skin into the bloodstream.

Each CLIMARA 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.

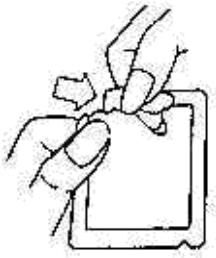
The CLIMARA patch should be applied once a week and worn continually for all 7 days. Remove the patch and apply a new one after 7 days. Only one CLIMARA patch should be worn at any one time during each 7-day time interval.

If you use the CLIMARA patch, and you still have your uterus, you should take a progestin medication (another hormone drug) regularly for a certain number of days to reduce the risk of endometrial hyperplasia or endometrial cancer.

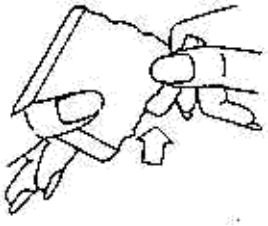
How to apply CLIMARA

Never cut the pouch with scissors – you might damage the patch inside.

To open the pouch, hold it vertically with the name CLIMARA facing you. Tear the pouch at the notch provided at the top of the left-hand corner, tearing from left to right.

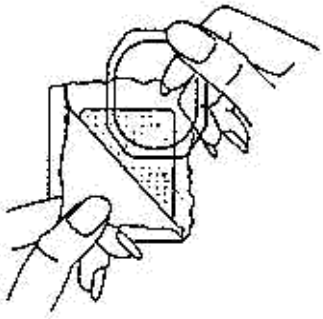


Next, open the right side of the pouch using the notch at the bottom of the right-hand corner and tear from bottom to top.



There is a silver-foil sticker securely attached to the inside of the pouch. This contains a moisture protectant. Do not remove it. The foil sticker does not contain medication. Discard it with the empty pouch.

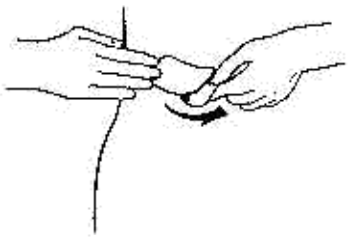
Carefully remove the patch.



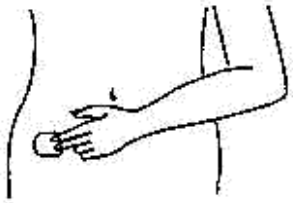
A diagonally-split protective plastic backing covers the adhesive side of the patch and must be removed before applying it. The patch itself is oval and translucent.

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, below). Discard the protective backing.

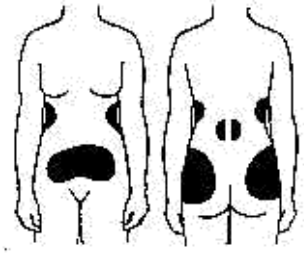


Apply firm pressure around the edges for about 10 seconds to make sure there are no air bubbles under the patch.



Where to apply CLIMARA

Apply the adhesive side of the patch to a clean dry area of the skin on the trunk of your body or buttocks. **Do not apply CLIMARA to your breasts due to potentially harmful effects on the breast tissue.** Avoid the waistline, since tight clothing may rub and remove the patch. The sites of application 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, above). Press the patch firmly in place with the fingers for about 10 seconds, making sure there is good contact, especially around the edges.



CLIMARA 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 against the patch.

When to apply CLIMARA

CLIMARA should be changed once a week. When changing the patch, remove the used CLIMARA patch and discard it. 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 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 will not affect the patch. In the unlikely event that a patch should fall off, a new patch should be applied for the remainder of the 7-day dosing interval.

Helpful Hints

If the patch falls off, such as in a very hot bath or shower, dry your skin completely and then apply a new patch (to a new area of skin) 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

Patches may stick better 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 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 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 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.

Overdose:

In case of drug overdose, contact a health care practitioner, hospital emergency department, or regional Poison Control Centre immediately, even if there are no symptoms

Overdosage of estrogen may cause nausea, breast discomfort, bloating or vaginal bleeding in women.

If you think that you have taken an overdose of CLIMARA, remove the patch.

Missed Dose:

If you forget to apply a patch, then apply a new patch and continue with your regular treatment schedule.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

The following side effects generally do not require medical attention, and will usually go away as your body adjusts to CLIMARA:

Common: breast pain, breast tenderness, bloating, dizziness, localized darkening of the skin, mood swings, redness or mild irritation under or around the patch, changes in genital bleeding pattern (including breakthrough bleeding and spotting), headache, weight gain

Uncommon: muscle cramps, breast enlargement,

If you think you are reacting poorly to CLIMARA or are having other problems, please tell your doctor.

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	
Common	Abdominal pain, nausea or vomiting		✓	
	Changes in body weight	✓		
	Heavy periods	✓		

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	
	Migraine headaches	✓		
	Persistent skin irritation	✓		
	Retention of fluid	✓		
	Unexpected vaginal bleeding		✓	
Uncommon	Breast lump		✓	
	Change in speech			✓
	Change in vision		✓	
	Crushing chest pain or chest heaviness			✓
Uncommon	Easy bruising, excessive nose bleeds, excessive heavy periods		✓	
	First migraine headache		✓	

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	
	Fluid retention or bloating persisting for more than 6 weeks		✓	
	High blood pressure		✓	
	Pain or swelling in the leg			✓
	Persistent sad mood			✓
	Rapid pulse or dizziness		✓	
	Sharp pain in the chest, coughing blood or sudden shortness of breath			✓
Uncommon	Skin redness, warmth, swelling, tenderness, pain or hardening of tissue around a vein		✓	

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	
	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			✓
	Vomiting		✓	
	Yellowing of the skin or eyes (jaundice)			✓

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

HOW TO STORE IT

Keep CLIMARA in its sealed pouch until you are ready to use it. Store at 15 - 30°C (room temperature). Do not freeze. Apply CLIMARA immediately upon removal from the protective pouch. CLIMARA should be kept out of the reach of children before and after use.

REPORTING SUSPECTED SIDE EFFECTS

Canada Vigilance Program

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 0701D
    Ottawa, ON K1A 0K9

  Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect™ Canada Website 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

For more information, please contact your health professional or pharmacist first, or Bayer Medical Information at 1-800-265-7382 or canada.medinfo@bayer.com.

This document plus the full product monograph, prepared for health professionals can be found at: http://www.bayer.ca or by contacting the manufacturer at the above-mentioned phone number and email address.

This leaflet was prepared by:

Bayer Inc.
2920 Matheson Boulevard East
Mississauga, Ontario L4W 5R6
Canada

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