

PATIENT INFORMATION
OESCLIM[®]
Estradiol Transdermal System

Please read this PATIENT INFORMATION carefully before you start using OESCLIM[®] (estradiol transdermal system) and each time you have your prescription refilled. This leaflet includes information on estrogens and progestins, how to use OESCLIM[®], and precautions to take when using OESCLIM[®]. This leaflet does not take the place of talking to your healthcare provider about your medical condition or your treatment. If you have any questions or concerns you should speak with your doctor or pharmacist.

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 *estrogen plus progestin* arm of 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 treatment with conjugated equine estrogens (an estrogen medication) and medroxyprogesterone acetate (a progestin medication).

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

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.

INTRODUCTION: What is OESCLIM®?

OESCLIM®

25, 37.5, 50, 75 or 100 microgrammes/24 hours

Transdermal System (patch)

OESCLIM® is a transdermal system which contains estradiol, a natural estrogen.

Your doctor has prescribed OESCLIM® for you after a careful review of your medical needs. Use it only as directed and do not give it to anyone else. Oesclim® 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 a pelvic exam. You should have a mammogram before starting treatment and at regular intervals as recommended by your doctor, and check your breasts regularly for lumps. 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 talk regularly with your doctor about whether you still need treatment with HRT.

INDICATIONS: OESCLIM® is approved for use in the following situations:

OESCLIM® has been given to you to relieve symptoms due to the lack of estrogen that occurs during or after menopause or because of surgery (see explanation below).

Estrogens

1. Estrogens are used to reduce moderate or severe menopausal symptoms. Your body normally makes estrogens and progestins (female hormones) mainly in the ovaries. Between the ages of 45-55, the ovaries gradually stop making estrogens. This leads to a decrease in body estrogen levels and a natural menopause (the end of monthly menstrual periods). If both ovaries are removed during an operation before natural menopause takes place, the sudden decrease in estrogen levels causes "surgical menopause".

Menopause is not a disease; it is a natural life event and different women experience menopause and its symptoms differently. Not all women experience the obvious symptoms of estrogen deficiency. When the estrogen levels begin decreasing, 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 flashes" or "hot flashes"). Using estrogen drugs can help the body adjust to lower estrogen levels and reduce these symptoms.

2. Estrogens are used to treat vulval and vaginal atrophy. Some women may also develop vulval or vaginal atrophy (itching, burning or dryness in or around the vagina, difficulty

or burning on urination) in association with menopause. These changes may be improved by estrogen therapy.

Progestins

Progestins used in hormone replacement therapy are similar to the female sex hormone progesterone. During the childbearing years, progesterone is responsible for the regulation of the menstrual cycle. The estradiol delivered by OESCLIM[®] 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 post-menopausal 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 developing endometrial cancer (cancer of the lining of the uterus).

The development of estrogen-mediated disorders of the uterus can be reduced if a progestin is given regularly for a certain number of days with your estrogen replacement therapy. Each cycle of progestin administration should include a periodic bleeding, whereby the inner lining of the uterus is regularly shed, thus protecting against endometrial hyperplasia.

If your uterus has been surgically removed, endometrial hyperplasia cannot occur and cyclic administration of a progestin is not necessary.

RESTRICTIONS ON USE: WHO SHOULDN'T TAKE OESCLIM[®]:

Certain medical conditions may be aggravated by estrogens; therefore estrogens should not be used at all or should be used with precaution under these conditions.

Estrogens should not be used during pregnancy. 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 physician at this time. If you take estrogen during pregnancy, there is a small risk of your unborn child having birth defects.

Estrogen should not be used if you are breast-feeding.

Before using OESCLIM[®], be sure to tell your doctor if you have ever had any of the following medical problems. OESCLIM[®] should not be used if you have any of the following conditions:

- < allergic or unusual reaction to any of the ingredients of OESCLIM[®] (see section called Pharmaceutical Information)
- < active liver disease
- < a personal history of breast cancer or endometrial cancer (cancer of the lining of the uterus)
- < undiagnosed or unusual vaginal bleeding
- < known or suspected pregnancy

- < stroke, heart attack, or coronary heart disease
- < migraine headaches
- < active or personal history of venous thromboembolism (blood clots in the large veins or lungs) or thrombophlebitis (inflammation of the veins)
- < partial or complete loss of vision due to blood vessel disease of the eye
- < porphyria (a disease of blood pigment)
- < endometrial hyperplasia (overgrowth of the lining of the uterus)

WARNINGS AND PRECAUTIONS

Breast Cancer

In the estrogen plus progestin arm of the WHI trial, among 10,000 women over a one-year period there were:

- 8 more cases of invasive breast cancer.

In the estrogen-alone arm of the WHI trial of women with prior hysterectomy, among 10,000 women over a one-year period there was:

- no meaningful difference in the rate of invasive breast cancer.

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 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.

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 of each month 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 required as part of hormone replacement therapy in women who have had a hysterectomy.

Heart Disease and Stroke

In the estrogen plus progestin arm of the WHI trial, among 10,000 women over a one- year period there were:

- 8 more cases of stroke
- 7 more cases of coronary heart disease.

In the estrogen-alone arm of the WHI trial of women with prior hysterectomy, among 10,000 women over a one-year period, there were/was:

- 12 more cases of stroke
- no meaningful difference in the rate of coronary heart disease.

Abnormal Blood Clotting

In the estrogen plus progestin arm of the WHI trial, among 10,000 women over a one- year period there were:

- 18 more cases of blood clots in the lungs and large veins.

In the estrogen-alone arm of the WHI trial of women with prior hysterectomy, among 10,000 women over a one-year period, there were:

- 7 more cases of blood clots in the lungs and large veins

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 involving women aged 65 and older.

In the estrogen plus progestin arm of the WHIMS, among 10,000 women over a one-year period there were:

- 23 more cases of probable dementia (loss of memory and intellectual function).

In the estrogen-alone arm of the WHIMS involving women with prior hysterectomy, among 10,000 women over a one-year period there was:

- no meaningful difference in the rate of probable dementia.

Benign Liver Tumours

Benign liver tumours have been associated with the use of combined estrogen and progestagen oral contraceptives. Although benign and rare, these tumours may rupture and cause death from internal abdominal bleeding. Such lesions have not yet been reported in association with other estrogen or progestagen preparations, but they should be considered if abdominal pain and tenderness, abdominal mass, or shock due to abnormal decrease in the volume of circulating blood occurs in patients receiving estrogen. Liver cell cancerous tumour has also been reported in women taking estrogen-containing oral contraceptives.

Before you use Oesclim[®] talk to your doctor or pharmacist if you:

- are taking any non-prescription medicines, including herbal products (St. John's Wort)
- 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
- drink alcohol
- smoke
- 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 a history of high cholesterol or high triglycerides (blood lipids)
- are pregnant or may be pregnant
- have had a hysterectomy (surgical removal of the uterus)
- have a history of depression
- are undergoing surgery or need long bed rest

ADVERSE EFFECTS

Like all medications, OESCLIM[®] may cause side effects. The most frequently reported side effect is redness or irritation under or around the patch. In clinical trials with OESCLIM[®], about 3 out of every ten women reported at least one local skin reaction to the patch at some point during their treatment. Out of all the patches applied in these studies, only 4 of every hundred times the patch was applied did reactions occur. These reactions included redness, itching, spots, burning and swelling.

The most commonly reported adverse reaction to OESCLIM[®] in clinical trials was application site reaction, which included redness, itching, spots, burning and swelling. Of the 22,239 applications in three clinical studies, 1,017 (4.6%) patches became detached. The second most frequent adverse reactions were symptoms of specific estrogen therapy intolerance, reported by 48.6% of patients in clinical trials. Approximately 30% of patients experienced signs of elevated estrogen levels, such as pain in the breast, irregular bleeding between periods and spotting.

The following effects have been reported in women using estrogens (these include estrogens used for birth control). Check with your doctor if these symptoms become troublesome.

- < nausea
- < retention of fluid
- < migraine headaches
- < localized darkening of the skin
- < breast tenderness and 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)
- < easy bruising, excessive nose bleeds, excessive heavy periods (may be signs of abnormal clotting)
- < 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 tumours)

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

- < irregular vaginal bleeding
- < intolerable breast tenderness

- < breast enlargement or lumps
- < pain or heaviness in the legs or chest
- < severe headaches
- < dizziness
- < 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:

- < narrowing of the throat
- < sudden shortness of breath
- < tightness of the chest or trouble breathing
- < coughing blood
- < rapid pulse or dizziness
- < tender or painful inflammation of the veins
- < pain or heaviness in the legs or chest
- < any other unusual symptom

HOW TO USE OESCLIM®

Your doctor will explain when to start using OESCLIM®. The OESCLIM® patches are applied twice weekly on the same days of each week. The system is changed every 3 or 4 days.

OESCLIM® is usually applied for 25 days out of 28 followed by 2 to 7 treatment-free days. Therefore 7 patches are required per cycle. To help you, we have included a timetable that marks the days of the week on which you should change your patch and the day you should remove the 7th patch (25th day of the cycle). Your next cycle starts with the next patch application.

If you still have your uterus, your doctor should prescribe another hormone drug (a progestogen) at the same time as the patch for at least the last 12 days of each treatment cycle with OESCLIM®.

Bleeding similar to menstrual bleeding may occur during the treatment-free period. This bleeding should be normal and slight.

Your doctor may prescribe the treatment using a different schedule that is better adapted to your condition. The system may be applied continuously with no treatment-free days.

It is important that you take your medication as your doctor has prescribed. Do not discontinue or change your therapy without consulting your doctor.

How OESCLIM[®] Works

Estradiol is the main estrogen produced by your ovaries prior to the menopause, and is the same estrogen that is in OESCLIM[®]. When applied to the skin, the OESCLIM[®] patch continuously releases small, controlled quantities of estradiol, which passes through your skin and into your bloodstream. The amount of estrogen prescribed depends on your body's needs. Your doctor may adjust the amount you get by prescribing another (different) patch size.

By providing estradiol, OESCLIM[®] offers relief from menopausal symptoms.

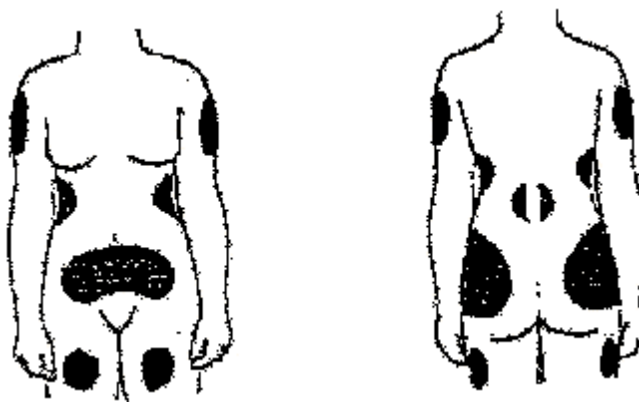
How and Where to Apply OESCLIM[®]

The site of application should be changed each time the patch is applied. However, each time you apply the patch you should always apply it to the same area of your body (i.e., if the patch is applied to the buttocks, move the patch from the right side to the left side).

1. **Preparing the skin:** In order for the patch to stick, the skin should be clean, dry and free of creams, lotions or oils. If you wish, you may use body lotion after the patch has been properly applied to the skin. The skin should not be irritated or broken, since this may alter the amount of hormone you get. Contact with water (bath, pool or shower) will not affect the patch, although very hot water or steam may loosen it and therefore should be avoided (see Helpful Hints).
2. **Where to Apply the OESCLIM[®] Patch:** The patch may be applied to the buttock, the torso (area under the arms at the elbow level, abdomen) or the upper part of the arm or thigh (see Fig. 1). Change the site of application each time you put a patch on. You can use the same spot more than once but **not twice in a row**.

Do not apply OESCLIM[®] to your abdomen, if a dose of OESCLIM[®] has been previously adjusted by your doctor with the patch applied to other sites of your body, as this might change the amount of hormone delivered.

Fig. 1



Avoid areas of the skin where clothing may rub the patch off or areas where the skin is very hairy or folded.

Also avoid areas where the patch is likely to be exposed to the sun since this may affect how the patch works.

Do not apply OESCLIM[®] to your breast, since this may cause unwanted effects and discomfort.

3. **Opening the Pouch:** Each OESCLIM[®] patch is individually sealed in a protective pouch. **Tear** open this pouch and remove the patch. Do not use scissors, as you may accidentally cut and destroy the patch.
4. **Removing the Liner:** The patch is made up of an adhesive part containing the active substance and a transparent protective film. The protective liner must be removed.

To separate the patch from the protective liner, lift a corner of the liner and peel it off the patch. Discard the protective liner. Avoid touching the adhesive. Press the sticky side on the skin and smooth down.

Apply the patch immediately after opening the pouch and removing the liner.

5. **Applying the OESCLIM[®] Patch:** Apply the adhesive side to the spot you have chosen. Check that the OESCLIM[®] system is sticking correctly: press firmly in place for about 10 seconds with the palm of your hand over its entire surface area.
6. **When and How to Remove the Patch:** To remove OESCLIM[®], simply lift up one edge and pull. The OESCLIM[®] patch should be changed twice weekly. Always change it on the same 2 days of the week. If you forget to change it at the scheduled time, there is no

cause for alarm. Just change it as soon as possible and **continue** to follow your usual schedule.

After you remove the patch fold it in half with the adhesive side inwards. **Throw it away out of the reach of children and pets.**

Apply a new OESCLIM[®] patch on a different spot of clean, dry skin.

SYMPTOMS AND TREATMENT OF OVERDOSAGE

Overdosage with estrogen may cause nausea, breast discomfort, fluid retention, bloating or vaginal bleeding in women.

In the case of overdosage, immediately remove the patch. Contact your doctor and/or your local Poison Control Centre.

PHARMACEUTICAL INFORMATION

Like most medicines OESCLIM[®] contains other substances in addition to estrogen. The other substances are: copolymer of ethylene vinyl acetate, dipropylene glycol, octyl dodecanol, ethyl cellulose, protective films made of foam and silicone-treated polyester.

STORAGE

OESCLIM[®] should be stored at room temperature (15–25EC). Avoid freezing. **Do not store unpouched.** OESCLIM[®] patches should be kept out of the reach of children and pets before and after use.

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 reapply the patch (to a new area of skin) and continue your regular schedule. If it does not stick, then apply a **new** patch and continue your regular schedule.

If hot baths, saunas or whirlpools are something you enjoy and you find that the patch is falling off, you may consider removing the patch **temporarily** while you are in the water. If you do remove the patch temporarily, the adhesive side of the patch should be placed on the protective liner that was removed when originally applying the patch. Wax paper may be used as an alternative to the liner. This prevents the contents of the patch from emptying by evaporation while you are not wearing it.

In addition to exposure to very hot water, 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 OESCLIM[®] 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 you may do:

- < choose the buttock as the site of application
- < change the site of application of the OESCLIM[®] patch every time a new patch is applied, usually twice weekly

Experience with OESCLIM[®] has shown that if you allow the patch to be exposed to the air for approximately 10 seconds after the protective liner has been removed, skin redness may not occur.

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

ALWAYS REMEMBER

Your doctor has prescribed OESCLIM[®] 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.

Product Identification

OESCLIM[®] 25 microgrammes/24 hours: A transdermal system with a surface area of 11 cm² containing 5 mg of estradiol-17 β .

OESCLIM[®] 37.5 microgrammes/24 hours: A transdermal system with a surface area of 16.5 cm² containing 7.5 mg of estradiol-17 β .

OESCLIM[®] 50 microgrammes/24 hours: A transdermal system with a surface area of 22 cm² containing 10 mg of estradiol-17 β .

OESCLIM[®] 75 microgrammes/24 hours: A transdermal system with a surface area of 33 cm² containing 15 mg of estradiol-17 β .

OESCLIM[®] 100 microgrammes/24 hours: A transdermal system with a surface area of 44 cm² containing 20 mg of estradiol-17 β .

Each system is contained in a heat-sealed paper/aluminium sachet.

REPORTING SUSPECTED SIDE EFFECTS

To monitor drug safety, Health Canada collects information on serious and unexpected effects of drugs. If you suspect you have had a serious or unexpected reaction to this drug you may notify Health Canada by:

toll-free telephone: 866-234-2345

toll-free fax: 866-678-6789

By email: cadrmp@hc-sc.gc.ca

By regular mail:

Canadian Adverse Drug Reaction Monitoring Program (CADRMP)

Marketed Health Products Safety and Effectiveness Information Division

Marketed Health Products Directorate

Health Canada

Tunney's Pasture, Address Locator: 0701C

Ottawa ON, K1A 0K9

NOTE: Before contacting Health Canada, you should contact your physician or pharmacist.

PALADIN LABS INC.

Montreal, Canada H4P 2T4

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