

### 4.3.2. Information for the Patient

#### INTRODUCTION

The Esclim® system that your doctor has prescribed for you releases small amounts of estradiol through the skin in a continuous way. Estradiol is the same hormone that your ovaries produce abundantly before menopause. The dose of estradiol you require will depend on your individual response. The dose is adjusted by the size of the Esclim system used; the systems are available in five sizes.

This leaflet describes when and how to use estrogens, and the risks and benefits of estrogen treatment.

Estrogens have important benefits but also some risks. You must decide, with your doctor, whether the risks to you of estrogen use are acceptable because of their benefits. If you use estrogens, 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 estrogens will depend on the reason for use.

**1. ESTROGENS INCREASE THE RISK OF CANCER OF THE UTERUS IN WOMEN WHO HAVE HAD THEIR MENOPAUSE (“CHANGE OF LIFE”).**

If you use any estrogen-containing drug, it is important to visit your doctor regularly and report any unusual vaginal bleeding right away. Vaginal bleeding after menopause may be a warning sign of uterine cancer. Your doctor should evaluate any unusual vaginal bleeding to find out the cause.

**2. ESTROGENS SHOULD NOT BE USED DURING PREGNANCY.**

Estrogens do not prevent miscarriage (spontaneous abortion) and are not needed in the days following childbirth. If you take estrogens during pregnancy, your unborn child has a greater than usual chance of having birth defects. The risk of developing these defects is small, but clearly larger than the risk in children whose mothers did not take estrogens during pregnancy. These birth defects may affect the baby's urinary system and sex organs. Daughters born to mothers who took DES (an estrogen drug) have a higher than usual chance of developing cancer of the vagina or cervix when they become teenagers or young adults. Sons may have a higher than usual chance of developing cancer of the testicles when they become teenagers or young adults.

## INFORMATION ABOUT ESCLIM

### *How The Esclim System Works*

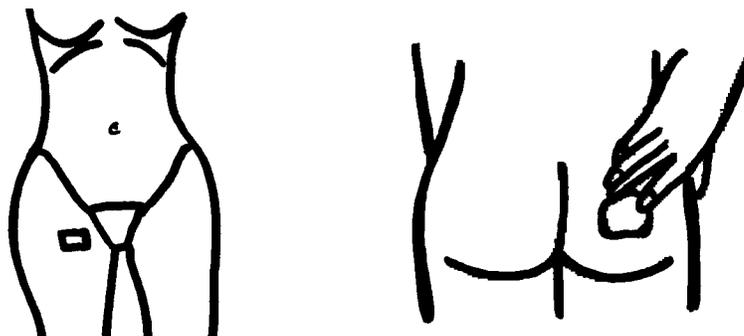
The Esclim system contains 17 $\beta$ -estradiol. When applied to the skin as directed below, the Esclim system releases 17 $\beta$ -estradiol continuously through the skin into the bloodstream.

### *How and Where to Apply the Esclim System*

Each Esclim system is individually sealed in a protective pouch. Tear open this pouch at the indentation (do not use scissors) and remove the system. The system is made up of a self-adhesive matrix, which contains the estradiol. The adhesive surface is covered by a transparent protective release liner. The adhesive side will be placed against your skin. This liner must be removed before applying the system



Remove the protective liner and discard it. Try to avoid touching the adhesive. Apply the adhesive side of the Esclim system to a clean, dry area of the skin on your upper arm, buttocks, or upper inner thigh. **Do not apply Esclim to your breasts or other parts of your body.** 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. The waistline should be avoided, since tight clothing may rub and remove the system. The system should be applied immediately after opening the pouch and removing the protective foil-liner. The system should be pressed firmly in place with the palm of the hand for about 10 seconds, making sure there is good contact, especially around the edges.



The Esclim system should be worn continuously until it is time to replace it with a new system. You may wish to experiment with different locations when applying the system, to find ones that are most comfortable for you and where clothing will not rub on the system.

### ***When to Apply the Esclim System***

The Esclim system should be changed every 3 to 4 days, two times per week, on the same two days of the week.

When changing the system, remove the used Esclim system. After removal, fold the patch in half so that the adhesive sides are together and discard. Any adhesive that might remain on your skin can be easily rubbed off. Then place the new Esclim system on a different skin site. (The same skin site should not be used again for at least 1 week after removal of the system.)

Contact with water when you are bathing, swimming, or showering will not affect the system. In the event that a system should fall off, the same system may be reapplied. If necessary, a new system may be applied. In either case, the original treatment schedule should be continued.

### **USES OF ESTROGEN**

(Not every estrogen drug is approved for every use listed in this section. If you want to know which of these possible uses are approved for the medicine prescribed for you, ask your doctor or pharmacist to show you the professional labeling. You can also look up the specific estrogen product in a book called the “Physician’s Desk Reference”, which is available in many book stores and public libraries. Generic drugs carry virtually the same labeling information as their brand name versions.)

#### **– To reduce moderate or severe menopausal symptoms.**

Estrogens are hormones made by the ovaries of normal women. Between ages 45 and 55, the ovaries normally stop making estrogens. This leads to a drop in body estrogen levels which causes the “change of life” or menopause (the end of monthly menstrual periods). If both ovaries are removed during an operation before natural menopause takes place, the sudden drop in estrogen levels causes “surgical menopause”.

When the estrogen levels begin dropping, 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 flushes”). Using estrogen drugs can help the body adjust to lower estrogen levels and reduce these symptoms. Most women have only mild menopausal symptoms or none at all and do not need to use estrogen drugs for these symptoms. Others may need to take estrogens for a few months while

their bodies adjust to lower estrogen levels. The majority of women do not need estrogen replacement for longer than six months for these symptoms.

- **To treat vulval and vaginal atrophy** (itching, burning, dryness in or around the vagina, difficulty or burning on urination) associated with menopause.
- **To treat certain conditions in which a young woman's ovaries do not produce enough estrogen naturally.**
- **To treat certain types of abnormal vaginal bleeding due to hormonal imbalance when your doctor has found no serious cause of the bleeding.**
- **To treat certain cancers in special situations, in men and women.**
- **To prevent thinning of bones.**

### **WHO SHOULD NOT USE ESTROGENS**

Estrogens should not be used:

- **During pregnancy (see Boxed Warning).**

If you think you may be pregnant, do not use any form of estrogen-containing drug. Using estrogens while you are pregnant may cause your unborn child to have birth defects. Estrogens do not prevent miscarriage.

- **If you have unusual vaginal bleeding which has not been evaluated by your doctor (see Boxed Warning).**

Unusual vaginal bleeding can be a warning sign of cancer of the uterus, especially if it happens after menopause. Your doctor must find out the cause of the bleeding so that he or she can recommend the proper treatment. Taking estrogens without visiting your doctor can cause you serious harm if your vaginal bleeding is caused by cancer of the uterus.

- **If you have had cancer.**

Since estrogens increase the risk of certain types of cancer, you should not use estrogens if you have ever had cancer of the breast or uterus, unless your doctor recommends that the drug may help in the cancer treatment. (For certain patients with breast or prostate cancer, estrogens may help).

- **If you have any circulation problems.**

Estrogen drugs should not be used except in unusually special situations in which your doctor judges that you need estrogen therapy so much that the risks are acceptable. Men and women with abnormal blood clotting conditions should avoid estrogen use (see Dangers of Estrogens, below).

– **When they do not work.**

During menopause, some women develop nervous symptoms or depression. Estrogens do not relieve these symptoms. You may have heard that taking estrogens for years after menopause will keep your skin soft and supple and keep you feeling young. There is no evidence for these claims and such long-term estrogen use may have serious risks.

**After childbirth or when breastfeeding a baby.**

Estrogens should not be used to try to stop the breasts from filling with milk after a baby is born. Such treatment may increase the risk of developing blood clots (see Dangers of Estrogens, below).

If you are breastfeeding, you should avoid using any drugs because many drugs pass through to the baby in the milk. While nursing a baby, you should take drugs only on the advice of your health care provider.

**DANGERS OF ESTROGENS**

– **Cancer of the uterus.**

Your risk of developing cancer of the uterus gets higher the longer you use estrogens and the larger doses you use. One study showed that after women stop taking estrogens, this higher cancer risk quickly returns to the usual level of risk (as if you had never used estrogen therapy). Three other studies showed that the cancer risk stayed high for 8 to more than 15 years after stopping estrogen treatment. Because of this risk, **IT IS IMPORTANT TO TAKE THE LOWEST DOSE THAT WORKS AND TO TAKE IT ONLY AS LONG AS YOU NEED IT.**

Using progestin therapy together with estrogen therapy may reduce the higher risk of uterine cancer related to estrogen use (but see Other Information, below).

If you have had your uterus removed (total hysterectomy), there is no danger of developing cancer of the uterus.

– **Cancer of the breast.**

Most studies have not shown a higher risk of breast cancer in women who have ever used estrogens. However, some studies have reported that breast cancer developed more often (up to twice the usual rate) in women who used estrogens for long periods of time (especially more than 10 years), or who used higher doses for shorter time periods.

Regular breast examinations by a health professional and monthly self-examination are recommended for all women.

– **Gallbladder disease.**

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

– **Abnormal blood clotting.**

Taking estrogens may cause changes in your blood clotting system. These changes allow the blood to clot more easily, possibly allowing clots to form in your bloodstream. If blood clots do form in your bloodstream, they can cut off the blood supply to vital organs, causing serious problems. These problems may include a stroke (by cutting off blood to the brain), a heart attack (by cutting off blood to the heart), a pulmonary embolus (by cutting off blood to the lungs), or other problems. Any of these conditions may cause death or serious long term disability. However, most studies of low dose estrogen usage by women do not show an increased risk of these complications.

**SIDE EFFECTS**

In addition to the risks listed above, the following side effects have been reported with estrogen use:

- Headaches
- Nausea and vomiting.
- Breast tenderness or enlargement.
- Enlargement of benign tumors (“fibroids”) of the uterus.

Retention of excess fluid. This may make some conditions worsen, such as asthma, epilepsy, migraine, heart disease. or kidney disease.

- A spotty darkening of the skin, particularly on the face.
- Skin irritation, redness or rash may occur at the application site.

**REDUCING RISK OF ESTROGEN USE**

If you use estrogens, you can reduce your risks by doing these things:

– **See your doctor regularly.**

While you are using estrogens, it is important to visit your doctor at least once a year for a check-up. If you develop vaginal bleeding while taking estrogens, you may need further evaluation. If members of your family have had breast cancer or if you have ever had breast lumps or an abnormal mammogram (breast x-ray), you may need to have more frequent breast examinations.

– **Reassess your need for estrogens.**

You and your doctor should reevaluate whether or not you still need estrogens at least every six months.

– **Be alert for signs of trouble.**

If any of these warning signals (or any other unusual symptoms) happen while you are using estrogens, call your doctor immediately:

Abnormal bleeding from the vagina (possible uterine cancer)

Pains in the calves or chest, sudden shortness of breath, or coughing blood (possible clot in the legs, heart, or lungs)

Severe headache or vomiting, dizziness, faintness, changes in vision or speech, weakness or numbness of an arm or leg (possible clot in the brain or eye)

Breast lumps (possible breast cancer; ask your doctor or health professional to show you how to examine your breasts monthly)

Yellowing of the skin or eyes (possible liver problem)

Pain, swelling, or tenderness in the abdomen (possible gallbladder problem)

Skin irritation

**OTHER INFORMATION**

1. Estrogens increase the risk of developing a condition (endometrial hyperplasia) that may lead to cancer of the lining of the uterus. Taking progestins, another hormone drug, with estrogens lowers the risk of developing this condition. Therefore, if your uterus has not been removed, your doctor may prescribe a progestin for you to take together with your estrogen.

You should know, however, that taking estrogens *with* progestins may have additional risks. These include:

- unhealthy effects on blood fats (especially a lowering of HDL blood cholesterol, the “good” blood fat which protects against heart disease);  
unhealthy effects on blood sugar (which might make a diabetic condition worse); and
- a possible further increase in breast cancer risk which may be associated with long-term estrogen use.

Some research has shown that estrogens taken *without* progestins may protect women against developing heart disease. However, this is not certain. The protection shown may have been caused by the characteristics of the estrogen-treated women, and not by the estrogen treatment itself. In general, treated women were slimmer, more physically active, and were less likely to have diabetes than the untreated women. These characteristics are known to protect against heart disease.

*You are cautioned to discuss very carefully with your doctor or health care provider all the possible risks and benefits of long-term estrogen and progestin treatment as they affect you personally.*

2. Your doctor has prescribed this drug for you and you alone. Do not give the drug to anyone else.
3. Keep this and all drugs out of the reach of children. In case of overdose, call your doctor, hospital or poison control center immediately.
4. This leaflet provides a summary of the most important information about estrogens. If you want more information, ask your doctor or pharmacist to show you the professional labeling. The professional labeling is also published in a book called the “Physicians Desk Reference”, which is available in book stores and public libraries. Generic drugs carry virtually the same labeling information as their brand name versions.

Store at 25°C (77°F); excursions permitted to 15°– 30°C (59°–86°F) . Do not store unpouched. Apply immediately upon removal from the protective pouch.

Rx only

Manufactured for Serono Laboratories, Inc., Randolph MA 02368 U.S.A.

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Made In France

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