PART III: CONSUMER INFORMATION

Pr SANDOZ ESTRADIOL DERM 50, 75 and 100
Estradiol hemihydrate (Estradiol-17β)

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

ABOUT THIS MEDICATION

What the medication is used for:
Sandoz Estradiol Derm is approved for use in the following situations:

- The Relief of Menopausal and Postmenopausal Symptoms

- To Prevent Osteoporosis
  Some women are more likely to develop osteoporosis after menopause than others. You should discuss risk factors for osteoporosis with your doctor.

  If you have been prescribed Sandoz Estradiol Derm only for the prevention of osteoporosis you should discuss other therapies with your doctor.

  In addition, you should discuss adequate diet, calcium and vitamin D intake, cessation of smoking and regular physical weight-bearing exercise with your doctor or pharmacist.

- Uses of Progestins
  If you have not had a hysterectomy (surgical removal of the uterus), estrogens should be prescribed in association with a progestin medication.

Sandoz Estradiol Derm 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:
Sandoz Estradiol Derm (estradiol-17β) is a type of treatment known as hormone replacement therapy (HRT). Sandoz Estradiol Derm is a patch which contains the estrogen hormone, estradiol. Estradiol is an estrogen produced by your ovaries before menopause (the end of monthly menstrual periods).

When applied to the skin, the Sandoz Estradiol Derm patch continually releases small, controlled quantities of estradiol, which pass through your skin and into your bloodstream

Your body normally makes estrogens and progestins (female hormones) mainly in the ovaries. Between ages 45 and 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 suffer 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 flushes**). Using estrogen drugs can help the body adjust to lower estrogen levels and reduce these symptoms.

Osteoporosis is a thinning of the bones that makes them weaker and allows them to break more easily. In osteoporosis, the bones of the spine, wrists and hips break most often. The bones of both men and women start to thin after about age 40, but women lose bone faster after menopause. Using estrogens after menopause slows down bone thinning and may prevent bones from breaking.

When it should not be used:
Sandoz Estradiol Derm (estradiol-17β) should not be used if you:

- have active liver disease.
- have a personal history of or currently have breast cancer or endometrial cancer (cancer of the uterus) or any other cancer which is sensitive to estrogens.
- have been diagnosed with endometrial hyperplasia (overgrowth of the lining of the uterus).
- have experienced undiagnosed or unexpected genital bleeding.
- have been diagnosed with porphyria (a disease of blood pigment).
- are pregnant or suspect 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 a history of coronary heart disease (including heart attack) or stroke.
- experience migraine headaches.
- have a history of or currently have blood clots.
- have active thrombophlebitis (inflammation of the veins).
- have had parial or complete loss of vision due to blood vessel disease of the eye.
- have had an allergic or unusual reaction to Sandoz Estradiol Derm or to any of its components.(See **What the medicinal ingredient is:** and **What the nonmedicinal ingredients are:)**

What the medicinal ingredient is:
Sandoz Estradiol Derm contains the estrogen hormone, estradiol.

What the nonmedicinal ingredients are:
The other substances are acrylic copolymers and tocopherol contained on a polyethylene terephthalate film.

What dosage forms it comes in:
Sandoz Estradiol Derm patch is available in 3 doses:
Sandoz Estradiol Derm 50 for continuous delivery of 50 mcg of estradiol per day.
Sandoz Estradiol Derm 75 for continuous delivery of 75 mcg of estradiol per day.
Sandoz Estradiol Derm 100 for continuous delivery of 100 mcg of estradiol per day.

The dose of Sandoz Estradiol Derm will be based on the reason for its use, as determined by your doctor. (Please see the section called **HOW TO USE Sandoz Estradiol Derm**).

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 postmenopausal women taking combined *estrogen plus progestin* compared to women taking placebo.

The results of the WHI trial indicated no difference in the risk of breast cancer in postmenopausal women with prior hysterectomy taking *estrogen-alone* compared to women taking placebo.

Estrogens 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 (HRT).

Women should have a mammogram (breast x-ray) 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 postmenopausal 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 generally required in women who have had a hysterectomy.

Ovarian cancer
In some studies, the use of *estrogen-alone* and *estrogen plus progestin* therapies for 5 or more years has been associated with an increased risk of ovarian cancer.

Heart Disease and Stroke
The results of the WHI trial indicated an increased risk of stroke and coronary heart disease in post-menopausal women taking combined *estrogen plus progestin* compared to women taking placebo.

The results of the WHI trial indicated an increased risk of stroke, but no difference in the risk of coronary heart disease in postmenopausal 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 postmenopausal 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 postmenopausal 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 reported to increase the risk of gallbladder disease requiring surgery.

Dementia
The Women's Health Initiative Memory Study (WHIMS) was a substudy of the WHI trial and indicated an increased risk of dementia (loss of memory and intellectual function) in postmenopausal women age 65 and over taking oral combined *estrogen plus progestin* compared to women taking placebo.

The WHIMS indicated no difference in the risk of dementia in postmenopausal women age 65 and over with prior hysterectomy taking oral *estrogen-alone* compared to women taking placebo.

BEFORE you use Sandoz Estradiol Derm 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 migraine headache.
- 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 been diagnosed with porphyria (a disease of blood pigment).
- are pregnant or may be pregnant.
- are breast feeding.
- have had a hysterectomy (surgical removal of the uterus).
- have a history of uterine fibroids or endometriosis.
- smoke.
- have a history of kidney disease, asthma or epilepsy (seizures).
- have a history of liver disease or liver tumours, jaundice (yellowing of the eyes and/or skin) or itching related to estrogen use or during pregnancy.
- have a history of bone disease (this includes certain 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 a history of high cholesterol or high triglycerides.
- have a history of depression.
- have been told that you have a condition called hereditary angioedema or if you have had episodes of rapid swelling of the hands, feet, face lips, eyes, tongue, throat (airway blockage), or digestive tract.
- have been diagnosed with lupus.
- have been diagnosed with hearing loss due to otosclerosis.

Remember that your doctor has prescribed this medicine only for you. Never give it to anyone else.

INTERACTIONS WITH THIS MEDICATION

Some medications can interfere with the action of Sandoz Estradiol Derm and Sandoz Estradiol Derm can interfere with the action of other medications.

Tell your doctor or pharmacist if you are taking any other medications including, prescription medications, over-the-counter medications, vitamins or herbal products. This particularly includes the following: anti-anxiety medicines (e.g. barbiturates, meprobamate), anti-epileptic medicines (.g. phenol barbital, phenytoin or carbamazepine), an anti-inflammatory medicine called phenylbutazone, antibiotics and other anti-infective medicines (e.g. rifampicin, rifabutin, vevirapine, efavirenz), and herbal medicines (e.g. St John's Wort).

PROPER USE OF THIS MEDICATION

Usual dose:
HOW TO USE Sandoz Estradiol Derm
Your doctor will explain when to start using Sandoz Estradiol Derm. The Sandoz Estradiol Derm patches are applied twice weekly on the same days of each week. Each patch should be worn continuously for 3 to 4 days. The dose of Sandoz Estradiol Derm will be based on the reason for its use, as determined by your physician. Your physician may adjust the dosage based on your response to treatment.

Estrogen is usually taken in a cyclic fashion (although your physician's instructions may be different depending upon your personal situation). This means that you would take estrogen on the first 21 or 25 days of the cycle, followed by 5 to 7 days without. Your next cycle starts with the next patch application.

Each box contains eight Sandoz Estradiol Derm patches. If your treatment is for less than 28 days of estrogen (cyclical therapy), you will have 1 or 2 patches leftover which can be used for the next month.

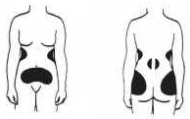
It is important that you take your medication as your physician has prescribed. Do not discontinue or change your therapy without consulting your physician first. You should talk regularly with your physician about how long you will need treatment with estrogen.

How and Where to Apply Sandoz Estradiol Derm
It is recommended that you change the site of application each time the patch is applied. However, each time you apply a 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 right side to left side, twice a week or more if there is any redness under the patch).

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) won't affect the patch, although very hot water or steam may loosen it and therefore should be avoided (see **Helpful Hints**).

Where to Apply the Sandoz Estradiol Derm Patch
The buttock is the preferred place to apply the patch. Other suitable application sites are the sides, hip, lower back or lower abdomen. 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**.

Figure #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 Sandoz Estradiol Derm to your breast, since this may cause unwanted effects and discomfort.

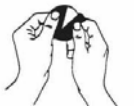
Opening the Pouch
Each Sandoz Estradiol Derm patch is individually sealed in a protective pouch. Tear open this pouch at the indented notch and remove the patch. Do not use scissors, as you may accidentally cut and destroy the patch.

Figure #2

Removing the Liner
One side of the patch has the adhesive that attaches to your skin. The adhesive is covered by a protective liner that must be removed.

To separate the patch from the liner, hold the patch with the protective liner facing you. Peel off one side of the protective liner and discard it. Try to avoid touching the sticky side of the patch with your fingers.

Figure #3



Using the other half of the liner as a handle, apply the sticky side of the patch to a dry area of intact skin on the trunk of the body. Press the sticky side on the skin and smooth down.

Fold back the remaining side of the edge of the protective liner and pull it across the skin. Avoid touching the adhesive.

Figure #4

Don't worry if the patch buckles slightly because you can flatten it out after the liner has been removed. Apply the patch soon after opening the pouch and removing the liner.

Applying the Sandoz Estradiol Derm Patch
Apply the adhesive side to the spot you have chosen. Press it firmly in place with the palm of your hand for about 10 seconds, then run your finger around the edge, making sure there is good contact with the skin.

When and How to Remove the Patch
The Sandoz Estradiol Derm patch should be changed twice weekly. Always change it on the same 2 days of the week.

After you remove the patch fold it in half with the adhesive sides inwards. Throw it away, safely out of reach of children or pets.

Any adhesive left on your skin will rub off easily. Apply a new Sandoz Estradiol Derm patch on a different spot of clean, dry skin.

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 still does not stick, then apply a new patch and continue with 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 alternate 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 Sandoz Estradiol Derm 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 buttock as the site of application
- change the site of application of the Sandoz Estradiol Derm patch every time a new patch is applied, usually twice weekly.

Experience with the estradiol patch 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 Sandoz Estradiol Derm for you after a careful review of your medical needs. Use it only as directed and do not give it to anyone else.

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

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

If more medication has been taken than what has been prescribed, remove the patch and contact either your doctor, hospital, or emergency department immediately.

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

Missed Dose
If you forget to change a patch at the scheduled time, apply a new patch as soon as you remember. No matter what day that happens, go back to changing the patch on the same day as your initial schedule.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

The following effects have been reported in women taking estrogens (these include estrogens used for birth control).

- genital bleeding/spotting
- headache
- breast tenderness
- bloating
- weight gain

Check with your doctor as soon as possible if any of the following occur: swelling of the lower legs, ankles, fingers or abdomen due to fluid retention (oedema) persisting for more than 6 weeks, change in weight, change in your sex drive, easy bruising, excessive nose bleeds, painful and/or heavy periods (may be signs of growth of fibroids in the uterus) change in vaginal discharge (may be sign that too much estrogen is taken), vaginal thrush (vaginal fungal infection with severe itching, vaginal discharge), intolerable breast tenderness, persistent or severe skin irritation, itching under or around the patch, reddening of the skin after the patch has been removed, hair loss, excessive hairiness, spotty darkening of the skin, particularly on the face or abdomen (chloasma), rash, itching, acne, dryness or discoloration of the skin, purple skin patches (purpura), headache, decline of memory or mental ability, uncontrollable jerky movements (chorea), contact lens discomfort, hearing loss, gall bladder disease (tendency to form gall stones).

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

Symptom/effect		Talk with your doctor or pharmacist		Stop taking drug and call your doctor or pharmacist
		Only if severe	In all cases	
Uncommon	Crushing chest pain or chest heaviness			✓
	Persistent sad mood			✓
	Sudden severe headache or worsening of headache, vomiting, dizziness, fainting, disturbance of vision or speech or weakness or numbness in an arm or leg			✓
	Migraine			✓
	Pain or swelling in the leg			✓
	Sudden partial or complete loss of vision			✓
	Sharp pain in the chest, coughing blood or sudden shortness of breath			✓
	Yellowing of the skin or eyes (jaundice)			✓
	Abdominal pain, nausea, or vomiting,		✓	
	Breast lump		✓	
	Unexpected vaginal bleeding, excessive heavy bleeding		✓	
	Increase in blood pressure		✓	

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

HOW TO STORE IT

Sandoz Estradiol Derm should be stored between 15 and 30°C. Protect from freezing. **Do not store it out of the pouch**.

Sandoz Estradiol Derm patches should be kept out of reach of children and pets before and after use.

REPORTING SUSPECTED SIDE EFFECTS

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

Online: www.healthcanada.gc.ca/medeffect
Toll-free phone: 1 866-234-2345
Toll-free fax: 1 866-678-6789
Postage Paid Mail: Canada Vigilance Program
Health Canada
AL 0701C
Ottawa ON K1A 0K9

NOTE: Should you require information related to the management of the side effect, please contact your health care provider. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

This document, plus the full Product Monograph prepared for health professionals, can be obtained by contacting the sponsor, Sandoz Canada Inc., at: 1-800-361-3062

or
by written request at:
145, Jules-Léger
Boucherville, (QC), Canada
J4B 7K8

or by e-mail at :

medinfo@sandoz.com

This leaflet was prepared by Sandoz Canada Inc.

Last revised: March 19, 2009