

## PART III: CONSUMER INFORMATION

<sup>PR</sup>Activelle®

**1 mg Estradiol and  
0.5 mg Norethindrone acetate**

**Film-coated tablets**

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

### ABOUT THIS MEDICATION

#### What the medication is used for:

Activelle® is approved for use in the following situations:

- ◆ To treat moderate to severe vasomotor symptoms (uncomfortable feelings of heat, flushing and sweating) that can occur as a result of the lower estrogen levels associated with menopause.
- ◆ To treat vulval and vaginal atrophy (changes in the vagina and/or external genitalia as a result of the low estrogen levels associated with menopause). Vulval and vaginal atrophy can contribute to symptoms such as itching, burning or dryness in or around the vagina, difficulty or burning during urination and pain while having sex.

Activelle® should only be used in women with an intact uterus.

Activelle® 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 start of 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:

The estrogen hormone is called estradiol (E2) and will help

relieve your menopausal symptoms. Estradiol is identical to the estrogen produced naturally by your body. Activelle® replaces the estrogen in your body, which decreases naturally at menopause. Estrogen therapy can help reduce or eliminate these symptoms.

The progestin hormone is called norethindrone acetate (NETA) and will help to reduce the risk of endometrial hyperplasia (stimulation of growth of the lining of the uterus), which could lead to cancer of the lining of the uterus (womb).

#### When Activelle® should not be used:

- If you have known hypersensitivity to this drug or any of its ingredients or to the components of the container
- If you have liver dysfunction or disease as long as liver function tests have failed to return to normal
- If you have known or suspected estrogen-dependent or progestin-dependent malignant neoplasia (e.g. endometrial cancer)
- If you have endometrial hyperplasia
- If you have known, suspected, or past history of breast cancer
- If you have undiagnosed abnormal genital bleeding
- If you are or think you might be pregnant
- If you have an active or past history of arterial thromboembolic disease (e.g. stroke, myocardial infarction and/or coronary disease)
- If you have an active or past history of confirmed venous thromboembolism (such as deep vein thrombosis or pulmonary embolism) or active thrombophlebitis
- If you have partial or complete loss of vision due to ophthalmic vascular disease
- If you have porphyria
- If you have migraine
- If you are breastfeeding

#### What the medicinal ingredients are:

1 mg Estradiol  
0.5 mg Norethindrone acetate

#### What the nonmedicinal ingredients are:

Hypromellose  
Lactose monohydrate  
Magnesium stearate  
Maize starch  
Talc  
Triacetin  
Copolydione

#### What dosage forms it comes in:

Activelle® is available in calendar dial-packs of 1x28 tablets

. Each tablet contains estradiol 1 mg (as the hemihydrate) and norethindrone acetate 0.5 mg.

## 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*.

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
- 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 postmenopausal women with prior hysterectomy taking *estrogen-alone* compared to women taking placebo.

Estrogens with or without progestins 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.

Regular breast examinations by a doctor and regular breast self-examinations are recommended for all women. You should review the 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).

The purpose of adding a progestin medication to estrogen therapy is 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

Prolonged use of hormone replacement therapy 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 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 sub-study 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 post-menopausal women age 65 and over with prior hysterectomy taking oral *estrogen-alone* compared to women taking placebo.

**BEFORE you use Activelle® 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 a history of migraine headaches;
- have 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 been diagnosed with porphyria (a disease of blood pigment);
- 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.

Other existing conditions you should discuss with your health professional include: lupus; very low calcium levels; thyroid problems; fluid retention; gallbladder disease; depression;

upcoming surgery and prolonged bed rest.

You should inform other doctors that you are taking Activelle® as certain laboratory tests may change during treatment.

**INTERACTIONS WITH THIS MEDICATION**

Tell your doctor or pharmacist if you are taking any other medications, including prescription medications, over-the-counter medications, vitamins or herbal products.

**Drugs that may interact with Activelle® include:**

- \$ drugs used for the treatment of epilepsy (e.g. phenobarbital, phenytoin and carbamazepine)
- \$ drugs used for tuberculosis (e.g. rifampicin, rifabutin)
- \$ drugs used for the treatment of HIV infections (e.g. nevirapine, efavirenz, ritonavir and nelfinavir)
- \$ herbal preparations containing St John’s Wort (*Hypericum perforatum*)

Drugs containing ketoconazole (a fungicide) may increase the effect of Activelle®.

Grapefruit juice may increase the effect of Activelle®.

**PROPER USE OF THIS MEDICATION**

You may begin treatment with Activelle® on any day that is convenient. However, if you switch from a sequential Hormone Replacement Therapy product, treatment should start right after withdrawal bleeding has ended.

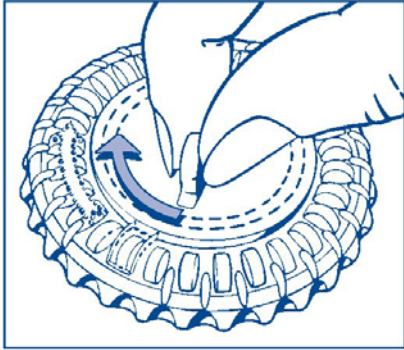
**Usual dose:**

Take 1 tablet once daily. Try to take Activelle® at the same time each day.

### How do I use the dial pack

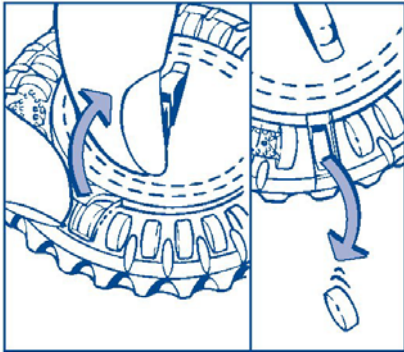
Activelle® is supplied in calendar dial packs of 28 white tablets. Follow these steps to use the calendar dial pack:

The first tablet to be taken is under the sealed opening in the see-through outer rim of the calendar dial-pack.



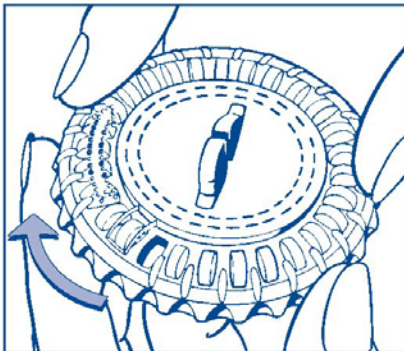
#### 1. Set the day reminder

Turn the inner disc to set the day of the week opposite the little plastic tab.



#### 2. How to take the first tablet

Break the plastic tab and tip out the first tablet.



#### 3. Every day

Simply move the transparent dial clockwise one space as indicated by the arrow. Tip out the next tablet.

**The transparent dial can only be turned after the tablet in the opening has been removed.**

#### Overdose:

In general, excessive doses of estrogen and progestin may result in nausea, vomiting, abdominal cramps, headache, dizziness, and general ill feeling (malaise). If you take too much of the drug, contact your doctor or local Poison Control Centre.

#### Missed Dose:

If you miss a day, do not double your dose to make up for the missed tablet. Instead take the next tablet, at the regular time, the next day. Forgetting a dose may increase the likelihood of breakthrough bleeding and /or spotting.

### SIDE EFFECTS AND WHAT TO DO ABOUT THEM

The following side effects may occur during your treatment with Activelle®:

Very common

- § Vaginal bleeding
- § Breast pain / tenderness

Common

- § Genital infection with a fungus or vaginal inflammation
- § Headache
- § Nausea (feeling sick)
- § Abdominal (stomach) pain
- § Back or neck pain
- § Pain in arms or legs
- § Weight increase

Some women who have used HRT have reported the following side effects while taking estrogen and/or progestin:

- § Vomiting, abdominal discomfort (pressure pain, cramps), bloating
- § Breast swelling or tenderness or enlargement
- § Irregular bleeding or spotting
- § Change in the amount of cervical secretion
- § Involuntary muscle spasms
- § Hair loss or abnormal hairiness
- § Acne
- § Increase or decrease in weight.

**IMPORTANT: PLEASE READ**

If you think you are experiencing a side effect of the treatment, talk to your doctor.

<b>SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM</b>				
Symptom / effect		Talk with your doctor or pharmacist		Stop taking drug and call your doctor or pharmacist
		Only if severe	In all cases	
<b>Common</b>	Abdominal pain, nausea or vomiting		✓	
	Pain in the leg			✓
	Unexpected vaginal bleeding		✓	
<b>Uncommon</b>	Breast lump		✓	
	Crushing chest pain or chest heaviness			✓
	Swelling of the leg			✓
	Persistent sad mood			✓
	Sharp pain in the chest, coughing blood or sudden shortness of breath			✓
	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			✓
	Yellowing of the skin or eyes (jaundice)			✓

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

**HOW TO STORE IT**

Keep this and all drugs out of the reach of children.

Keep Activelle® at room temperature, (15° - 25°C) away from heat and humidity. Store in a dry place. Protect from light by keeping the dial-pack inside the outer carton.

Do not store any of your medications near the cooking area of the kitchen, the shower area of the bathroom or the glove compartment of your car as the temperature in these locations may go above normal room temperature from time to time. Do not store the calendar dial-pack in the refrigerator. Do not use Activelle® after the expiry date printed on the label of the calendar dial-pack and on the carton.

**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 by:

By toll-free telephone: 866-234-2345  
 By toll -free fax: 866-678-6789  
 Online: [www.healthcanada.gc.ca/medeffect](http://www.healthcanada.gc.ca/medeffect)  
 By email: [CanadaVigilance@hc-sc.gc.ca](mailto:CanadaVigilance@hc-sc.gc.ca)

By regular mail:  
 Canada Vigilance National Office  
 Marketed Health Products Safety and Effectiveness Information Bureau  
 Marketed Health Products Directorate  
 Health Products and Food Branch  
 Health Canada  
 Tunney's Pasture, 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 before notifying Canada Vigilance. 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, Novo Nordisk Canada Inc., at: 1-800-465-4334

This leaflet was prepared by Novo Nordisk Canada Inc.

IMPORTANT: PLEASE READ

Manufactured by:  
For more information contact:  
Novo Nordisk Canada Inc.  
Mississauga, Ontario, Canada  
L4W 5L6  
**1 • 800 • 465 • 4334**  
[www.novonordisk.ca](http://www.novonordisk.ca)

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Last revised: **March 6, 2008**