

## PART III: CONSUMER INFORMATION

<sup>Pr</sup>Activelle® *LD*

**0.5 mg Estradiol and  
0.1 mg Norethindrone acetate**

**Film-coated tablets**

**This leaflet is part III of a three-part "Product Monograph" published when Activelle® *LD* 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® *LD*. Contact your doctor or pharmacist if you have any questions about this drug.**

### ABOUT THIS MEDICATION

#### What the medication is used for:

Activelle® *LD* is used to relieve moderate to severe vasomotor symptoms such as hot flushes and sweats in menopausal women with intact uteri.

Activelle® *LD* 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® *LD* replaces the estrogen in your body, which decreases naturally at menopause.

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® *LD* 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

#### What the medicinal ingredients are:

0.5 mg Estradiol  
0.1 mg Norethindrone acetate

#### What the nonmedicinal ingredients are:

Hydroxypropylcellulose  
Hypromellose  
Lactose monohydrate  
Magnesium stearate  
Maize starch  
Talc  
Triacetin

#### What dosage forms it comes in:

Activelle® *LD* is available in calendar dial-packs of 1x28 tablets each tablet contains estradiol 0.5 mg (as the hemihydrate) and norethindrone acetate 0.1 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 post-menopausal 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 post-menopausal 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**

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 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 post-menopausal 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 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.

**BEFORE you use Activelle® LD 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® LD as certain laboratory tests may change during treatment.

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

Grapefruit juice may increase the effect of Activelle® LD.

**PROPER USE OF THIS MEDICATION**

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

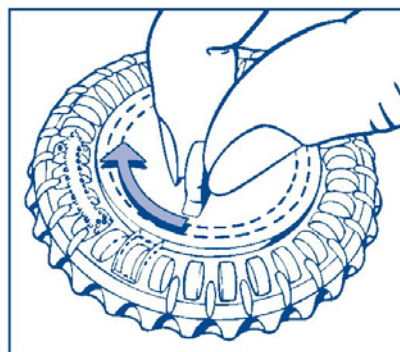
**Usual dose:**

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

**How do I use the dial pack?**

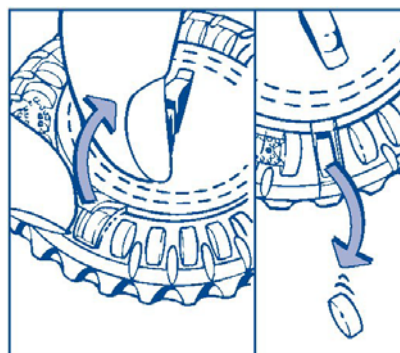
Activelle® LD is supplied in calendar dial-packs of 28 white tablets. Follow these steps to use the calendar dial-pack:

The first tablet to be taken is under the sealed opening in the see-through outer rim of the 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**

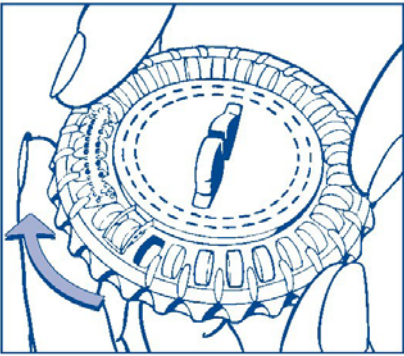
Break the plastic tab and tip out the first tablet.

**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® LD 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, zidovudine and zalcitabine)
- herbal preparations containing St John's Wort (*Hypericum perforatum*).



**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.

- Breast swelling 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.

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

**SIDE EFFECTS AND WHAT TO DO ABOUT THEM**

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

**Very common**

- Vaginal bleeding

**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
- Endometrial thickening (enlarged lining of the womb)

Breast discomfort and tenderness were reported by less than 2% of subjects treated with Activelle® LD.

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;

**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	
<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® LD, contact your doctor or pharmacist.*

## HOW TO STORE IT

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

Keep Activelle® LD 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® LD 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 toll-free telephone: 1-866-234-2345**

**By toll -free fax: 1-866-678-6789**

**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 healthcare 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 at 1-800-465-4334

This leaflet was prepared by Novo Nordisk Canada Inc.

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