PART III: CONSUMER INFORMATION

Pr ANGELIQ®

Drospirenone and estradiol-17β tablets

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

ABOUT THIS MEDICATION

What the medication is used for:

ANGELIQ is approved for use in postmenopausal women with an intact uterus:

- to reduce and relieve vasomotor symptoms (hot flashes and night sweats)
- to treat moderate and severe dryness, itching, and burning in and around the vagina associated with menopause

ANGELIQ 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. Unexpected or undiagnosed vaginal bleeding should be investigated by your doctor.

You should carefully discuss the risks and benefits of hormone replacement therapy (HRT) with your doctor.

You and your healthcare provider should talk regularly about whether you still need treatment with ANGELIQ to control these problems.

If you have had a hysterectomy (surgical removal of the uterus), endometrial hyperplasia cannot occur and administration of a progestin is not necessary. Therefore, ANGELIQ **should not** be used by women who have had a hysterectomy.

What it does:

Estrogens are hormones made by a woman's ovaries. The ovaries normally stop making estrogens when a woman is between 45 to 55 years old. This drop in body estrogen levels causes the "change of life" or menopause (the end of monthly menstrual periods). Sometimes, 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 strong feelings of heat and sweating ("hot flashes" or "hot flushes"). In some women, the symptoms are mild, and they will not need estrogens. In other women, symptoms can be more severe. You and your health care provider should talk regularly about whether you still need treatment with ANGELIQ.

The estradiol in ANGELIQ 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 postmenopausal 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 endometrial cancer (cancer of the lining of the uterus). The risk of endometrial hyperplasia is reduced if a progestin is given together with estrogen replacement therapy.

When it should not be used:

You **should not** use ANGELIQ if you:

- have active liver disease
- have a personal history of breast cancer or endometrial cancer (cancer of the lining of the uterus)
- have or have had liver tumors
- have severe kidney disease
- have a very high level of fatty acids in the blood called hypertriglyceridemia
- have been diagnosed with endometrial hyperplasia (overgrowth of the lining of the uterus)
- have experienced undiagnosed or abnormal genital bleeding
- have a history of heart attack, heart disease, or stroke
- experience migraine headaches
- have a personal history of blood clots or active thrombophlebitis (inflammation of the veins)
- are at high risk of having a blood clot including if you were born with certain blood clotting abnormalities

- have had partial or complete loss of vision due to blood vessel disease of the eye
- are pregnant or think you may be pregnant. (Since pregnancy may be possible early in menopause while you are still having spontaneous periods, the use of nonhormonal 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 had a hysterectomy (surgical removal of the uterus)
- have had an allergic or unusual reaction to estrogen, progestin, or any component of ANGELIQ
- have adrenal disease

What the medicinal ingredients are:

Drospirenone and estradiol-17β

What the nonmedicinal ingredients are:

Corn starch, ferric oxide pigment, hydroxypropylmethyl cellulose, lactose monohydrate, macrogol, magnesium stearate, modified starch, povidone, talc, and titanium dioxide.

What dosage forms it comes in:

ANGELIQ (drospirenone and estradiol-17β) is available in a 28-day regimen. Each blister pack contains 28 dark pink film-coated tablets. Each tablet contains 1 mg drospirenone and 1 mg estradiol-17β.

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 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 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.

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.

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). The purpose of adding a progestin medication to estrogen therapy is to reduce the risk of endometrial hyperplasia.

You should discuss risk factors for endometrial hyperplasia and endometrial carcinoma with your doctor. You should 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.

Heart Disease and Stroke

The results of the WHI trial indicated an increased risk of stroke and coronary heart disease in postmenopausal 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 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 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.

Certain medical conditions may be aggravated by estrogens or progestins. Therefore, these hormones should either not be used at all or should be used with caution under these conditions.

BEFORE you use ANGELIQ talk to your doctor or pharmacist if you:

- are taking any other prescription or nonprescription medications (including herbal products such as St. John's wort). There are some medicines which may interfere with the effects of ANGELIQ and ANGELIQ may interfere with the effects of other medicines.
- are currently on daily, long-term treatment for a chronic condition with any of the medications listed below:
    - nonsteroidal anti-inflammatory drugs (NSAIDs) when taken long-term and for the treatment of arthritis or other problems (eg, ibuprofen, naproxen, or others)
    - potassium-sparing diuretics (spironolactone and others)
    - potassium supplements
    - Angiotensin converting enzyme (ACE) inhibitors and Angiotensin-II receptor antagonists for the treatment of high blood pressure (eg, captopril, enalapril, lisinopril, losartan, valsartan, irbesartan, or others)
    - heparin
- 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 endometrial hyperplasia (overgrowth of the lining of the uterus)
- 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
- 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
- if you are undergoing surgery or need long bed rest
- 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 been diagnosed with high prolactin levels or prolactinoma
- have a history of high cholesterol or high triglycerides
- are pregnant or may be pregnant
- are breast feeding
- have had a hysterectomy (surgical removal of the uterus)
- smoke
- have a history of depression
- have been told that you have a condition called hereditary angioedema or if you have had episodes of swelling in body parts such as hands, feet, face, lips, eyes, tongue, throat (airway blockage), or digestive tract
- have been diagnosed with hearing loss due to otosclerosis
- have been diagnosed with lupus

INTERACTIONS WITH THIS MEDICATION

Drugs that may interact with ANGELIQ include:

- anticoagulants, antidiabetic agents
- drugs used for the treatment of certain heart diseases or high blood pressure (eg, diltiazem, verapamil)
- drugs used for the treatment of HIV infections and Hepatitis C Virus infections (e.g., nelfinavir, ritonavir, ritonavir-boosted protease inhibitors, boceprevir, telaprevir, nevirapine)
- barbiturates, hydantoins, carbamazepine, meprobamate, phenylbutazone, primidone, phenytoin, oxcarbazepine, topiramate, felbamate or rifamicin
- antibiotics (eg, erythromycin, clarithromycin, penicillin, tetracycline)
- antifungals (eg, griseofulvin, fluconazole, itraconazole, ketoconazole, voriconazole)
- antivirals (ritonavir)

Alcohol, grapefruit juice, and St. John's wort may also interact with ANGELIQ.

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

PROPER USE OF THIS MEDICATION

Usual dose

ANGELIQ is very simple to take – one pill, once a day, every day. You can take ANGELIQ any time of day, with or without food. However, it's usually easier to plan to take it at the same time each day.

Estrogens should be used only as long as needed. You and your doctor should talk regularly about whether you still need treatment with ANGELIQ.

Overdose

Symptoms: Overdosage with estrogen or progestin containing products may cause nausea, breast discomfort, fluid retention, bloating, vaginal bleeding, depressed mood, tiredness, acne, and hirsutism (excessive hair growth).

In case of drug overdose, contact health care practitioner, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

Missed Dose

If you forget a tablet, take it as soon as you remember and take the next one at your regular time. If you have missed your tablet by more than 24 hours, leave the tablet in the pack and take the next one at the regular time. Do not take a double dose to make up for a missed one. If you forget several tablets, you may get some slight vaginal bleeding or spotting.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

During treatment you may experience some vaginal bleeding at unexpected times (breakthrough bleeding and spotting). These symptoms normally lessen with continued treatment. If they don't, contact your doctor. About one in five women using ANGELIQ experience breast pain.

Women who have used ANGELIQ have reported the side effects listed below. The reported side effects have been divided into groups, depending on how commonly they occurred.

Common effects (may affect up to 1 in 10 users)

- abdominal pain or bloating, or pain in your fingers or toes
- feeling sick (nausea) or feeling unusually tired or weak
- headache, mood swings, hot flashes, nervousness
- enlarged or lumpy breasts
- increased size of fibroids in the womb (uterus)
- growth of cells at the neck of the womb
- vaginal discharge
- breakthrough bleeding
- depression

Uncommon effects (may affect up to 1 in 100 users)

- back, pelvic, chest or joint pain
- migraine, high blood pressure, fast or irregular heartbeats (palpitations), varicose veins, blood clots in the veins, inflammation of veins usually in the legs, widening of blood vessels (which may make you feel faint)
- stomach or intestinal problems, diarrhea, constipation, vomiting, flatulence, increased appetite, change in laboratory tests
- fluid retention leading to swelling of parts of the body, increase or decrease in weight
- high levels of fat in the blood
- muscle cramps
- difficulty sleeping, dizziness, decreased sex drive, difficulty concentrating, pins and needles, increased sweating, anxiety, dry mouth, spinning sensation (vertigo)
- difficulty breathing
- unusual hair loss or hair growth, skin problems, a feeling of fullness and tenderness in the breasts, breast cancer
- changes to your sense of taste
- vaginal infections, womb and neck of the womb (cervix) problems, painful periods, fluid filled sacs in the ovaries (ovarian cysts), urinary tract infections, loss of bladder or bowel control
- abnormal vision

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	
Common	Abdominal pain, nausea or vomiting		✓	
	Breast lump		✓	
	Persistent sad mood			✓
	Unexpected vaginal bleeding		✓	
Uncommon	Vomiting		✓	
	Pain or swelling in the leg			✓
Rare	Crushing chest pain or chest heaviness			✓
	Sharp pain in the chest, coughing blood or sudden shortness of breath			✓
	Sudden partial or complete loss of vision			✓

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	
	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 ANGELIQ, contact your doctor or pharmacist.

HOW TO STORE IT

ANGELIQ tablets should be stored at room temperature, between 15°C and 30°C. Do not refrigerate or freeze. Please note the expiry date on the pack. Do not use after this date.

ANGELIQ should be kept out of the reach of children and pets.

REPORTING SUSPECTED SIDE EFFECTS

Canada Vigilance Program

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

- Report online at www.healthcanada.gc.ca/medeffect
- Call toll-free at 1-866-234-2345
- Complete a Canada Vigilance Reporting Form and:
  - Fax toll-free to 1-866-678-6789, or
  - Mail to: Canada Vigilance Program
    Health Canada
    Postal Locator 0701E
    Ottawa, ON K1A 0K9

Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect™ Canada Web site at www.healthcanada.gc.ca/medeffect.

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

MORE INFORMATION

For more information, please contact your health professional or pharmacist first, or Bayer Medical Information at 1-800-265-7382 or canada.medinfo@bayer.com.

This document plus the full product monograph, prepared for health professionals can be obtained by contacting the manufacturer at the above-mentioned phone number and email address.

This leaflet was prepared by:

Bayer Inc.
2920 Matheson Boulevard East
Mississauga, Ontario L4W 5R6
Canada

Last revised: February 17, 2016