

PART III: CONSUMER INFORMATION

Pr **DUAVIVE™**
conjugated estrogens and bazedoxifene
modified release tablets

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

ABOUT THIS MEDICATION**What the medication is used for:**

DUAVIVE is used in menopausal women with a uterus (womb) to treat moderate to severe symptoms of menopause (hot flashes).

DUAVIVE should not be used by women who have had surgical removal of the uterus (hysterectomy).

DUAVIVE should not be taken with a progestin, additional estrogen, or an additional selective estrogen receptor modulator (such as raloxifene).

DUAVIVE 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 therapy (HT) with your doctor. You should regularly talk with your doctor about whether you still need treatment with HT.

It is important to talk about smoking cessation and adequate diet with your doctor before starting **DUAVIVE**.

What it does:

Estrogens are hormones made by a woman's ovaries. The ovaries normally stop making estrogens when a woman is between 45 and 55 years old. This drop in body estrogen levels causes the "change of life" or menopause (the end of monthly menstrual periods). Menopause occurs when a woman has not had a menstrual period for 12 months in a row. Sometimes both ovaries are removed during an operation before natural menopause take place. The sudden drop in estrogen levels causes "surgical menopause".

Every woman experiences menopause differently. When the estrogen levels begin dropping, some women experience very uncomfortable vasomotor 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 to take medicines. In other women, symptoms can be more severe.

Estrogen in **DUAVIVE** helps to relieve vasomotor symptoms ("hot flashes", "hot flushes"). Since estrogen may also stimulate

the growth of the lining of the uterus, **DUAVIVE** also contains bazedoxifene, a selective estrogen receptor modulator, to help reduce the risk of overgrowth of the lining of the uterus (endometrial hyperplasia).

When it should not be used:

You should **not take DUAVIVE** if you:

- Have a blood clot or if you have a history of blood clots (including those in the leg, lungs, veins or eyes) which required treatment by a doctor.
- have a known allergy (hypersensitivity) to estrogens, bazedoxifene or to any of the ingredients in **DUAVIVE**.
- have unexpected or unusual vaginal bleeding.
- have or have had breast cancer.
- have or have had hormone-dependent cancer.
- currently have liver problems or have had estrogen-related liver problems.
- endometrial hyperplasia
- have known blood disorders that may give you a greater risk of blood clots (such as protein C, protein S, or antithrombin deficiency).
- are or may become pregnant. **DUAVIVE** may cause harm to your unborn child if taken during pregnancy.
- are breastfeeding your child. It is not known if **DUAVIVE** passes into breast milk or what effect it might have on the baby.
- If you have partially or completely lost vision due to blood vessel disease of the eye.

What the medicinal ingredient is:

Conjugated estrogens and bazedoxifene acetate.

What are the nonmedicinal ingredients:

ascorbic acid, black iron oxide, calcium phosphate tribasic, hydroxyethylcellulose, hydroxypropyl cellulose, hypromellose, lactose monohydrate, magnesium stearate, maltitol, microcrystalline cellulose, poloxamer 188, polyethylene glycol, polydextrose, povidone, powdered cellulose, propylene glycol, red iron oxide, sucrose, sucrose palmitic acid ester, titanium dioxide.

What dosage forms it comes in:

DUAVIVE is a pink, oval-shaped tablet, imprinted with 0.45/20. It contains conjugated estrogens 0.45 mg and 20 mg bazedoxifene as bazedoxifene acetate as the active ingredients.

WARNINGS AND PRECAUTIONS**Serious Warnings and Precautions**

The Women's Health Initiative (WHI) is a large clinical study that assessed the benefits and risks of oral *estrogen-alone* therapy compared with placebo (a pill with no active ingredients) in postmenopausal women.

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 stroke and blood clots in the large veins with the use of estrogen-alone therapy.
- Estrogens should not be used for the prevention of heart disease or stroke.
- Estrogens 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 no difference in the risk of breast cancer in post-menopausal 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 HT.

Women should have a mammogram before starting HT and at regular intervals during treatment as recommended by their doctor.

Regular breast examinations by a doctor and regular breast self-examination 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 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).

DUAVIVE contains conjugated estrogens and bazedoxifene. Bazedoxifene reduces the risk of endometrial hyperplasia that can occur with the conjugated estrogens component. Women taking **DUAVIVE** should not take additional estrogens as this may increase the risk of endometrial hyperplasia.

Women taking **DUAVIVE** who are overweight are also at risk for endometrial hyperplasia.

Women taking **DUAVIVE** should not take progestins.

Ovarian Cancer

Some studies have indicated that taking *estrogen-alone* for 5 or more years may increase the risk of ovarian cancer.

Heart Disease and Stroke

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 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.

Taking **DUAVIVE** may increase your risk of getting blood clots. While infrequent, these clots can cause serious medical problems, disability or death. Speak with your doctor to see if you are at increased risk for blood clots.

Bazedoxifene, a component of **DUAVIVE**, is a Selective Estrogen Receptor Modulators or SERM. SERMS are known to increase the risk of blood clots.

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 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 DUAVIVE talk to your doctor or pharmacist if:

- 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.
- you currently have or have had certain cancers, such as uterine or breast cancer. If you have or have had cancer, talk with your doctor about whether you should use **DUAVIVE**.
- have a personal or family history of blood clots, or a personal history of heart disease or stroke

- have a history of high triglycerides (a kind of fat in the blood) or high cholesterol.
- Currently have or have a history of liver diseases or liver tumours, jaundice (yellowing of the eyes and/or skin) or itching related to estrogen use or during pregnancy.
- have experienced any unusual or undiagnosed vaginal bleeding
- have a history of uterine fibroids or endometriosis
- have a history of migraine headache
- have a history of high blood pressure
- 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)
- are pregnant or may be pregnant
- have had a hysterectomy (surgical removal of the uterus)
- smoke
- have been diagnosed with lupus
- have been diagnosed with hearing loss due to otosclerosis
- have been told that you have a condition called hereditary angioedema or if you have had episodes of rapid deep swelling of the hands, feet, face, lips, eyes, tongue, throat (airway blocked), or digestive tract.

DUAVIVE is not indicated for use in children.

INTERACTIONS WITH THIS MEDICATION

Tell your doctor about all the medicines you take. This includes prescription medications, over-the-counter medications, in particular, other hormonal treatments (eg. other estrogens, progestins) used for menopausal symptom relief and osteoporosis, vitamins and herbal supplements.

Drugs that may interact with DUAVIVE include:

- antifungals (drugs used to treat fungal infections, such as ketoconazole and itraconazole)
- antibiotics (such as erythromycin, clarithromycin and rifampin)
- medications bought without a prescription or natural health products (such as, St. John's Wort or Grapefruit juice)
- antiviral medications (such as, ritonavir).
- anticonvulsants (drugs that treat seizures, such as phenobarbital, carbamazepine and phenytoin)

DUAVIVE may interfere with laboratory testing

PROPER USE OF THIS MEDICATION

Take DUAVIVE as instructed by your doctor and pharmacist. Do not increase or decrease the dose or stop taking DUAVIVE without first talking to your doctor.

Usual dose:

Take one DUAVIVE tablet by mouth daily. Tablets should be swallowed whole with fluid and not be divided, crushed, chewed or dissolved in the mouth. You can take DUAVIVE at any time of the day, with or without food. Take DUAVIVE at about the same

time every day to help you remember to take DUAVIVE regularly.

If you take supplemental calcium and /or vitamin D, it may be taken at the same time as DUAVIVE.

DUAVIVE should not be taken with progestin, additional estrogens or selective estrogen receptor modulators (e.g. raloxifene)

Overdose:

If you think you have taken too much DUAVIVE, contact your healthcare professional, hospital emergency department or regional poison control centre immediately, even if there are no symptoms.

Missed Dose:

In the event you miss a dose of DUAVIVE, take it as soon as you remember. However, if it is almost time to take your next dose of DUAVIVE, skip the dose you missed and only take your next scheduled dose. Do not take two doses of DUAVIVE at the same time.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Like all medicines, DUAVIVE can have side effects. For most patients these side effects are likely to be minor and temporary. However, some may be serious. **Serious side effects have occurred in women taking DUAVIVE during clinical studies.** At this time it is unknown whether or not these side effects were caused by the use of DUAVIVE. **Talk with your doctor if you get any of the following symptoms or if they become severe:**

- **High blood pressure:** headache, vision disorders, nausea, and vomiting.
- **Tachycardia:** rapid heart rate.
- **Palpitations:** heart skips a beat.
- **Edema:** swelling of the hands or feet.

Other side effects may include:

- heartburn, gas, diarrhea, change in appetite
- dizziness, motion sickness, fatigue, drowsiness
- back, muscle, neck pain, muscle spasms, non-cardiac chest pain
- breast pain, tenderness, cyst, or swelling
- pain when urinating, urinary tract infection, incontinence, vaginal infection
- cramps or spotting
- fever, bronchitis, cold-like symptoms, sinus headache
- seasonal allergy
- acne, hair loss, dry skin, itchiness, rash, reduced sense of touch/sensation
- deafness, ear discomfort
- eye disorder, pain, swelling, pus or bleeding, vision changes, double vision, seeing flashes of light, drooping eyelid
- nosebleeds
- toothache, mouth and gum discomfort or sores, change in taste of food

- feeling hot, temperature intolerance
- mood swings, panic attacks, abnormal dreams

If any of these affects you severely, tell your doctor, nurse or pharmacist.

Abnormal blood and PAP or cervical smear test results have occurred in women taking **DUAVIVE**. Your doctor will decide when to perform tests and will interpret the results.

The following serious side effects have been reported with the use of conjugated estrogens or the combination of conjugated estrogens and progesterin. These side effects may occur with the use of **DUAVIVE** (conjugated estrogens and bazedoxifene).

SERIOUS SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Symptom / possible side effect	Talk with your doctor or pharmacist		Stop taking drug and call your doctor or pharmacist
	Only if severe	In all cases	
Abdominal pain, nausea or vomiting		√	
Breast lump		√	
Crushing chest pain or chest heaviness			√
Pain or swelling in 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			√
Unexpected vaginal bleeding		√	
Yellowing of the skin or eyes (jaundice)			√

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

HOW TO STORE IT

Store at controlled room temperature, 20° to 25°C, excursions permitted to 15-30 °C. Keep **DUAVIVE** in the blister until you are ready to take it to protect the tablet from moisture. It is recommended that **DUAVIVE** not be placed in pill boxes or pill organizers. After opening the foil pouch the **DUAVIVE** blisters came in, **DUAVIVE must be used within 45 days**. Keep out of reach of children.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on **Adverse Reaction Reporting** (<https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada.html>) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

This document plus the full product monograph, prepared for health professionals can be found at:

<http://www.pfizer.ca>

or by contacting the sponsor, Pfizer Canada Inc., at: 1-800-463-6001

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