

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

Pr **DUAVIVE™**

Conjugated estrogens and bazedoxifene modified release tablets

Read this carefully before you start taking **DUAVIVE** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **DUAVIVE**.

Serious Warnings and Precautions

In postmenopausal women taking estrogen-alone who had prior surgery to remove the uterus (called a hysterectomy), there is an increased risk of:

- stroke (bleeding or blood clot in the brain), and
- deep vein thrombosis (blood clots in the deep veins of the leg or arm)

Estrogens, like that in **DUAVIVE**, should:

- not be used to prevent heart disease or stroke.
- be used at the **lowest effective dose** and for the **shortest period of time** possible. You should have regular medical check-ups.

What is **DUAVIVE** used for?

DUAVIVE is used to treat moderate to severe symptoms of menopause (hot flashes). These are called vasomotor symptoms. **DUAVIVE** is used in adult women who are in menopause and still have a uterus.

DUAVIVE should not be taken with other medications that contain progestin or estrogen, or with selective estrogen receptor modulator (such as raloxifene).

How does **DUAVIVE** work?

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.

DUAVIVE is a hormone therapy (HT) that contains 2 ingredients that have different functions. The estrogen in **DUAVIVE** helps to relieve hot flashes or hot flushes (called vasomotor symptoms) that are

associated with menopause. Since estrogen may also stimulate the lining of the uterus to grow, DUAVIVE also contains bazedoxifene to help reduce the risk of overgrowth of the lining of the uterus (a condition called endometrial hyperplasia).

What are the ingredients in DUAVIVE?

Medicinal ingredients: Conjugated estrogens and bazedoxifene acetate

Non-medicinal 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

DUAVIVE comes in the following dosage forms:

Tablet: 0.45 mg conjugated estrogens and 20 mg bazedoxifene (as bazedoxifene acetate)

Do not use DUAVIVE if:

- you have a blood clot or you have a history of blood clots (including those in veins of the leg (deep vein thrombosis), lungs (pulmonary embolism), or eyes.
- you were previously diagnosed as having a stroke, heart attack (myocardial infarction), or heart disease.
- you are allergic (hypersensitivity) to estrogens, bazedoxifene or to any of the ingredients in DUAVIVE.
- you have unexpected or unusual vaginal bleeding.
- you have or have had breast cancer.
- you have or have had estrogen-dependent cancer.
- you currently have liver problems.
- you have thickening of the endometrium (endometrial hyperplasia)
- you have known blood disorders that may give you a greater risk of blood clots (such as protein C, protein S, or antithrombin deficiency).
- you are, think you are or may become pregnant. DUAVIVE may cause harm to your unborn child if taken during pregnancy.
- you are breastfeeding your child. It is not known if DUAVIVE passes into breast milk or what effect it might have on the baby.
- you have partially or completely lost vision due to blood vessel disease of the eye.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take DUAVIVE. Talk about any health conditions or problems you may have, including 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
- you currently have or have had certain cancers, such as uterine or breast cancer
- 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

- have or have a history of liver disease or liver tumours, jaundice (yellowing of the eyes and/or skin)
- have a history of itching related to estrogen use or during pregnancy
- have experienced any unusual or undiagnosed vaginal bleeding
- have a history of fibroids inside your womb (uterus) or growth of the womb outside of your womb (endometriosis)
- have a history of migraine headache
- have a history of high blood pressure
- have a history of kidney disease
- have a history of 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 in your blood
- 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 abnormal bone growth in your ear (otosclerosis)
- are taking thyroid hormone replacement therapy
- have lactose intolerance. This is because DUAVIVE contains lactose. Tell your doctor if you have lactose intolerance or one of the following rare hereditary diseases:
 - galactose intolerance
 - Lactase deficiency
 - Glucose-galactose malabsorption
- 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
- are taking progestin. Women taking DUAVIVE should not take progestins

Other warnings you should know about:

- **Breast Cancer**
 - Estrogens should not be taken by women who have a personal history of breast cancer.
 - Talk to your healthcare professional before starting HT if you have:
 - a family history of breast cancer or have had breast lumps, breast biopsies or abnormal mammograms (breast x-rays)
 - Never had a baby before or had your first full-term pregnancy at an older age
 - You are overweight
 - You started menstruating at an early age
- **Overgrowth of the lining of the uterus and cancer of the uterus:**
 - Taking estrogen-only therapy by post-menopausal women who still have a uterus increases your risk of excessive thickening of the lining of the-womb (endometrial hyperplasia) and cancer of the lining of the womb (endometrial cancer).
 - If you are overweight and taking DUAVIVE, you are also at risk for endometrial hyperplasia.

- If you experience bleeding or spotting during your treatment, or after you have stopped taking DUAVIVE, your healthcare professional will do tests to find out why. You may need a biopsy of your endometrium (lining of the womb).
- **Ovarian Cancer** Taking estrogen-alone for 5 or more years may increase the risk of ovarian cancer.
- **Abnormal Blood Clotting:** Taking DUAVIVE can increase your risk of developing blood clots in your large veins. You should discuss risk factors for blood clots with your healthcare professional since blood clots can be life threatening or cause serious disability. Talk to your healthcare professional if:
 - you or a family member has had blood clots
 - you smoke
 - you are overweight

The risk of blood clots is increased as you get older. It is also temporarily increased:

- if you are inactive for long periods of time
- 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.

If you are going to have a major surgery, your healthcare professional may recommend you temporarily stop take DUAVIVE about 4 weeks before the procedure.

When travelling where you will have long periods of inactivity, be sure to move about periodically.

- **Gallbladder Disease:** Your risk of developing gallbladder disease that requires surgery is increased when taking estrogens.

Dementia: A clinical study showed no reduction in the risk of developing dementia (memory loss) in women with no uterus (due to hysterectomy) who were over 65 years of age and taking oral estrogen.

Check-ups and testing: You will have regular visits with your healthcare professional, before and during your treatment. They will:

- Do a physical exam and blood work (which may include a pregnancy test) before you begin 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 healthcare professional.
- Do regular follow-up exams including a breast exam and blood pressure check at least once a year to identify side effects associated with the use of DUAVIVE. Your first follow-up visit should be within 3 to 6 months of starting treatment.
- Advise you to regularly check your own breasts. Talk to your healthcare professional if you are unsure on the technique to use.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with DUAVIVE:

- medicines used to treat fungal, bacterial or viral infections such ketoconazole, itraconazole, erythromycin, clarithromycin, rifampin and ritonavir
- an herbal treatment for depression called St. John's Wort
- medicines used to treat seizures, such as phenobarbital, carbamazepine and phenytoin
- a medicine used in the treatment of bipolar disorder called lamotrigine
- a medicine used to treat mild pain called phenylbutazone
- medicines to treat or prevent blood clots
- medicines to treat diabetes
- medicines to treat high blood pressure

Do not eat grapefruit or drink grapefruit juice during your treatment with DUAVIVE. This is because it could affect the way medicine works and may lead to side effects.

DUAVIVE may interfere with laboratory testing.

How to take DUAVIVE:

- Take exactly as your healthcare professional has told you. Check with your healthcare professional if you are not sure.
- Take 1 tablet per day, with or without food. Take **DUAVIVE** at about the same time every day to help you remember to take **DUAVIVE** regularly.
- Swallow tablet whole. Do not divide, crush, chew or dissolve in the mouth.
- Do not increase or decrease the dose or stop taking DUAVIVE without first talking to your healthcare professional.
- If you take calcium and /or vitamin D supplements, these may be taken at the same time as DUAVIVE.

Usual dose: 1 tablet per day

Overdose:

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

Taking too much estrogen might cause nausea, vomiting, dizziness, drowsiness, fatigue, breast discomfort, fluid retention, abdominal pain, bloating or vaginal pain in women.

Missed Dose:

- If you miss a dose of DUAVIVE, take it as soon as you remember.
- If it is almost time to take your next dose, skip the missed dose. Take your next dose at the regular time.
- Do not take two doses of DUAVIVE at the same time.

What are possible side effects from using DUAVIVE?

These are not all the possible side effects you may have when taking DUAVIVE. If you experience any side effects not listed here, tell your healthcare professional.

- Acne, hair loss, changes in hair growth or texture, dry skin, itchiness, rash, reduced sense of touch/feel.
- Itching at the anus, hemorrhoids, painful sores that appear in the mouth, painful swallowing, armpit pain.
- Back, muscle, neck pain; chest pain (not related to heart problems), muscle spasms.
- Breast pain, tenderness, cyst or swelling.
- Bunion.
- Inflammation of a fluid-filled sac that cushions a joint (bursitis).
- Pain in the flank pain, groin, pubic area, extremities.
- Joint swelling.
- Abnormal fluid-filled sacs in joints in the spine (synovial cyst).
- Tendonitis.
- Change in appetite.
- Brown patches on certain areas of the skin (chloasma).
- Changes in hair growth and texture.
- Nail problems.
- Skin sensitivity or an unusual reaction when your skin is exposed to UV radiation from sunlight or a tanning bed.
- Reddened skin and a rash usually on the nose and cheeks.
- Skin lesion or nodule.
- Hives.
- Cramps, spotting.
- Deafness, ear discomfort.
- Diarrhea, gas.
- Dizziness.
- Eye problems, pain, swell, pus or bleeding, vision changes, double vision, seeing flashes of light, drooping eyelids.
- Fatigue, drowsiness.
- Feeling hot, feeling cold.
- Fever, bronchitis, cold-like symptoms, sinus headache.
- Increased sex drive.
- Heartburn.
- Liver pain.
- Low blood pressure.
- Infections.
- Mood swings, panic attacks, abnormal dreams.
- Motion sickness.
- Nosebleeds.
- Slow-growing, fatty lump in the skin.
- Moles.
- Non-cancerous skin growth.

- Pain when urinating, trouble controlling when you pee, urinary tract infection, vaginal infection.
- Seasonal allergy.
- Sudden abdominal pain due to a blockage in a bile duct, inflammation of the gallbladder or gallstones. Surgery may be needed.
- Toothache, mouth and gum discomfort or sores, taste changes.

DUAVIVE can cause abnormal blood and PAP or cervical smear test results. Your healthcare professional will decide when to do these tests and will interpret the results.

Serious side effects and what to do about them			
Symptom /possible side effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
VERY COMMON			
Abdominal pain, nausea or vomiting		√	
Edema of the hands and feet: swelling caused by fluid trapped in your body's tissues	√		
COMMON			
Depression: persistent sad mood			√
Hypertension: high blood pressure			√
Myocardial infarction (heart attack): crushing chest pain or chest heaviness			√
Palpitations/ tachycardia: feelings or sensations that your heart is pounding or racing (palpitations), a heart rate over 100 beats a minute (tachycardia)			√
UNCOMMON			
Affective disorder (a mood disorder): persistent sadness, elation, irritability, mood swings		√	
Blood clot of the eye: sudden partial or complete loss of vision			√
Breast abnormalities (including breast cancer): lumps or discharge from the breast, changes in the nipple		√	
Colonic polyp (abnormal tissue growths on the lining of the large intestine): constipation, diarrhea, blood in stool or in the toilet bowl after a bowel movement, fatigue		√	
Deep vein thrombosis (blood clot in the deep veins of the leg or arm): pain or swelling in the leg			√

Serious side effects and what to do about them			
Symptom /possible side effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
Jaundice: yellowing of the skin or eyes, dark urine, light coloured stool, itching all over your body			√
Hematemesis: vomiting up blood		√	
Malignant melanoma (a type of skin cancer): spot on skin or mole that change in size, shape or colour or has irregular borders		√	
Pleurisy (inflammation of the tissue surrounding the lungs): chest pain, cough, difficulty breathing, fever, shortness of breath		√	
Pulmonary embolism (blood clot in the lungs): sharp pain in the chest, coughing blood or sudden shortness of breath			√
Stroke (bleeding or blood clot in the brain): sudden severe headache or worsening of headache, vomiting, dizziness, fainting, disturbance of vision or speech or weakness or numbness in an arm or leg			√
Thyroid cancer: lump in the neck, trouble breath or swallowing, pain when swallowing, loss of your voice		√	
Thyroid problems (underactive thyroid, autoimmune thyroiditis, goiter): fatigue, sleepiness, sensitivity to cold, dry skin, weakness, pain, swelling at the front of the neck		√	
RARE			
Endometrial hyperplasia or endometrial cancer (abnormal growth or cancer of the lining of the uterus): unexpected vaginal bleeding not associated with a period or after menopause, menstrual bleeding that is heavier or lasts long than normal, abnormal blood-tinged discharge from the vagina, pain in the pelvis		√	

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

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/adverse-reaction-reporting.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.

Storage:

Store at 20° to 25°C. Keep **DUAVIVE** in the blister until you are ready to take it to protect the tablet from moisture. Avoid using pill boxes or pill organizers to store DUAVIVE. After opening the foil pouch the **DUAVIVE** blisters came in, use DUAVIVE within 45 days.

Keep out of reach and sight of children.

If you want more information about DUAVIVE:

- Talk to your healthcare professional.
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website: (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html>); the manufacturer's website (<http://www.pfizer.ca>), or by calling 1-800-463-6001.

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