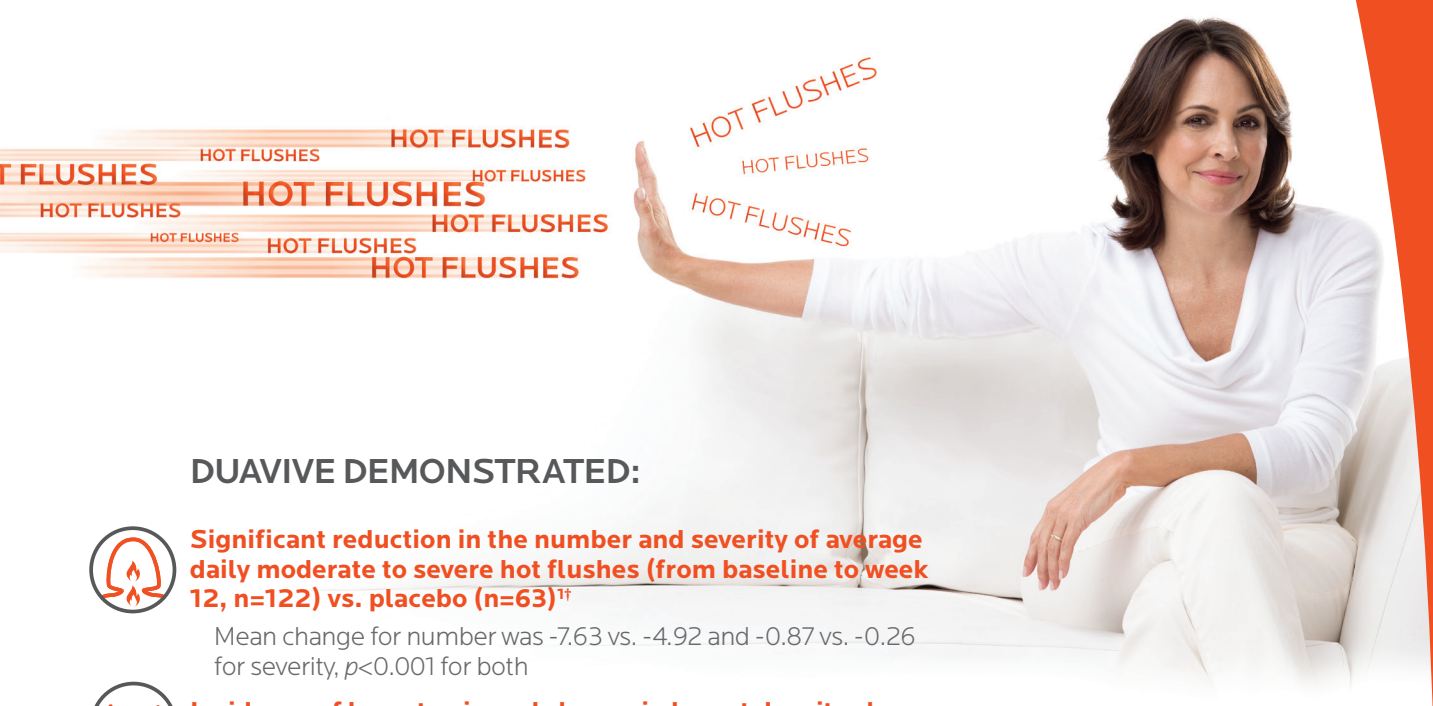
PROGESTIN-FREE HORMONE THERAPY
FOR WOMEN WITH A UTERUS*

Pr DUAVIVE™

FOR THE TREATMENT OF MODERATE TO SEVERE VASOMOTOR SYMPTOMS ASSOCIATED WITH MENOPAUSE



DUAVIVE DEMONSTRATED:

Significant reduction in the number and severity of average daily moderate to severe hot flushes (from baseline to week 12, n=122) vs. placebo (n=63)[1†]

Mean change for number was -7.63 vs. -4.92 and -0.87 vs. -0.26 for severity, $p<0.001$ for both

Incidence of breast pain and change in breast density shown not to be significantly different from placebo

Incidence of breast pain at Weeks 9-12: 9% vs. 6%, respectively[1‡]

Mean percentage change in breast density from baseline after 1 year of treatment: -0.49 vs. -0.51, respectively

Low incidence of endometrial hyperplasia[1§]

In clinical studies up to 2 years' duration, <1% incidence of endometrial hyperplasia or malignancies observed (0% and 0.30% at year 1, 0.68% at year 2)

Cumulative amenorrhea rates similar to placebo[1‡§]

In SMART 1, cumulative amenorrhea at Year 1 was 83% in women treated with DUAVIVE, similar to placebo (85%)

In SMART 5, cumulative amenorrhea at Year 1 (Cycle 1 to 13th), was 88% with DUAVIVE, similar to placebo (84%)

Improved sleep adequacy and menopause-specific quality of life total score vs. placebo (secondary endpoints)[2†]

Adjusted mean change from baseline in sleep adequacy score at week 12: 16.53 vs. 1.07, respectively, $p<0.001$

The parameters of sleep quantity, somnolence, snoring and shortness of breath were not significantly different from placebo[2]

Mean change from baseline in MENQOL total score at Week 12: -1.6 vs. -1.0, respectively, DUAVIVE demonstrated $p<0.001$

1 tablet. 1 strength. Once daily.

TISSUE SELECTIVE ESTROGEN COMPLEX (TSEC)[1]*

A purposeful pairing of conjugated estrogens (CE) with the selective estrogen receptor modulator (SERM) bazedoxifene (BZA)[1]*

Indications and clinical use:
DUAVIVE is indicated in women with a uterus for the treatment of moderate to severe vasomotor symptoms associated with menopause. DUAVIVE should not be taken with a progestin, additional estrogens or selective estrogen receptor modulators (SERMs).
Not recommended for women >75 years of age.
Not indicated for pediatric use.

Contraindications:
- Active or past history of confirmed venous thromboembolism (VTE) or active thrombophlebitis
- Active or past history of arterial thromboembolic disease
- Hypersensitivity (for example, angioedema, anaphylaxis) to estrogens, bazedoxifene or to any ingredient in the formulation or component of the container
- Undiagnosed abnormal genital bleeding
- Known, suspected, or past history of breast cancer
- Known or suspected estrogen-dependent malignant neoplasia
- Liver dysfunction or disease as long as liver functions tests have failed to return to normal
- Endometrial hyperplasia
- Known protein C, protein S, or antithrombin deficiency or other known thrombophilic disorders
- Known or suspected pregnancy, women who may become pregnant, and nursing mothers
- Partial or complete loss of vision due to ophthalmic vascular disease

Most serious warnings and precautions:

Risk of stroke and deep vein thrombosis: estrogen-alone therapy (mean age 63.6 years). Therefore, estrogens with or without progestins:
- Should not be prescribed for primary or secondary prevention of cardiovascular diseases
- Should be prescribed at the lowest effective dose and for the shortest period possible for the approved indication

Other relevant warnings and precautions:
- Possible risk of ovarian cancer
- Monitor blood pressure with hormone replacement therapy use
- Caution in patients with otosclerosis
- Caution in women with pre-existing endocrine and metabolic disorders
- Caution in patients with rare hereditary galactose intolerance
- Abnormal vaginal bleeding
- May increase pre-existing uterine leiomyomata
- May exacerbate previous diagnosis of endometriosis
- May increase the risk of VTE
- Risk of gallbladder disease
- Caution in patients with history of liver and/or biliary disorders
- Caution in women with hepatic hemangiomas
- Angioedema
- Caution in women with systemic lupus erythematosus
- Cerebrovascular insufficiency
- May exacerbate epilepsy
- Fluid retention
- Not recommended in renal impairment
- Not recommended in premenopausal women
- Women with higher BMIs may exhibit decreased bazedoxifene exposure which may be associated with an increased risk of endometrial hyperplasia

For more information:
Please consult the Product Monograph at http://pfizer.ca/pm/en/DUAVIVE.pdf for important information relating to adverse reactions, drug interactions and dosing information, which have not been discussed in this piece. The Product Monograph is also available by calling 1-800-463-6001.

* Clinical significance has not been established.

† SMART 2: 12-week, double-blind, placebo-controlled trial in 318 women who had 7 moderate to severe hot flushes/day or ≥50/week at baseline who were randomized to DUAVIVE (n=127), CE 0.625 mg/BZA 20 mg (n=128), or placebo (n= 63). Primary endpoint assessed efficacy of vasomotor symptom relief. Secondary endpoints included: number of mild, moderate, and severe hot flushes, sleep parameters [Medical Outcomes Study (MOS) scale], and overall Menopause Specific Quality of Life (MENQOL). Mean daily number of moderate and severe hot flushes at baseline: 10.3 for DUAVIVE, 10.5 for placebo. Baseline MENQOL total scores: DUAVIVE 4.46, placebo 4.42.

‡ SMART 1: 24-month, double-blind, placebo- and active-controlled dose-ranging trial of 3397 women who were randomized to DUAVIVE (n=433), raloxifene 60 mg or placebo. Women took calcium and vitamin D (Caltrate 600 + D™) daily. Primary endpoint was the incidence of endometrial hyperplasia; secondary endpoint was the treatment of vasomotor symptoms.

§ SMART-5: 12-month, double-blind, placebo- and active-controlled trial of 1843 women who were randomized to DUAVIVE (n=445), CE 0.625 mg/BZA 20 mg (n=474), BZA 20 mg (n=230), conjugated estrogens 0.45 mg /medroxyprogesterone acetate (MPA) 1.5 mg (n=220) or placebo (n=474). Women also took calcium, 600 mg and vitamin D, 400 IU daily.

Reference: 1. DUAVIVE Product Monograph. Pfizer Canada ULC, January 16, 2019. **2.** Utian WH *et al.* Bazedoxifene/conjugated estrogens and quality of life in postmenopausal women. *Maturitas.* 2009;63:329-35.

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INNOVATIVE MEDICINES CANADA PAAB

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Pr DUAVIVE™
0.45 MG CONJUGATED ESTROGENS/ 20 MG BAZEDOXIFENE ACETATE MODIFIED RELEASE TABLETS