



# Pfizer Inc. Announces FDA Approval Of DUAVEETM (conjugated estrogens/ bazedoxifene) For The Treatment Of Moderate- To-Severe Vasomotor Symptoms (Hot Flashes) Associated With Menopause And The Prevention Of Postmenopausal Osteoporosis [1]

Thursday, October 03, 2013 - 12:14pm

DUAVEE is the first and only therapy to pair conjugated estrogens with an estrogen agonist/antagonist, also known as a selective estrogen receptor modulator (SERM) [2]

NEW YORK, N.Y., October 3 - Pfizer Inc. (NYSE: PFE), a leader in the development of treatments for menopausal symptoms, is pleased to announce that the United States Food and Drug Administration (FDA) has approved DUAVEETM (conjugated estrogens/bazedoxifene) 0.45mg / 20mg tablets, a novel therapy for women with a uterus, for the treatment of moderate-to-severe vasomotor symptoms associated with menopause and the prevention of postmenopausal osteoporosis [1]. When prescribing solely for the prevention of postmenopausal osteoporosis, therapy should only be considered for women at significant risk and non-estrogen medication should be carefully considered [1]. DUAVEE is a once daily tablet taken orally. It is recommended that all menopausal hormone therapies, including DUAVEE, be used for the shortest duration consistent with treatment goals and risks for the individual woman [1]. Pfizer anticipates

that DUAVEE will be available in the U.S. in the first quarter of 2014. This is the first approval of DUAVEE in any country worldwide.

There are approximately 33 million women in the United States between the ages of 45-59, [3] and the average age of menopause in the U.S. is 51 [4]. Based on survey data, an estimated 50% of postmenopausal women experience moderate-to-severe vasomotor symptoms, commonly known as “hot flashes.” [5]

“We know that many women currently experiencing menopausal symptoms are not receiving treatment and have not talked to their doctor about hormone therapy [6]. It is clear that the menopause dialogue needs to improve,” said Gail Cawkwell, MD, PhD, Vice President, Pfizer Medical Affairs. “The approval of DUAVEE, an important, novel and effective treatment, presents a new opportunity for women and their doctors to discuss appropriate options for managing hot flashes and preventing osteoporosis.”

## **About DUAVEE**

Estrogens have been used as hormonal treatments for over 60 years to help manage menopausal symptoms [7]. Using estrogen alone can increase the chance of developing cancer of the uterine lining. When treating postmenopausal women with a uterus, estrogens have traditionally been combined with a progestin. This can decrease the risk of hyperplasia (the thickening of the endometrium), which may be a precursor to cancer of the uterine lining [7].

DUAVEE is the first and only therapy to pair conjugated estrogens (CE) with an estrogen agonist/antagonist also known as a selective estrogen receptor modulator (SERM) [2]. DUAVEE uses bazedoxifene - instead of a progestin - to help protect the uterine lining against hyperplasia that may result from estrogen-alone treatment [1].

Bazedoxifene was specifically selected to be studied as the SERM in DUAVEE because of its unique pharmacologic profile and mechanism of action, as demonstrated by pre-clinical studies that looked at a number of different SERMs [8]. The pairing of CE with bazedoxifene enables DUAVEE to work selectively in different tissues to activate estrogen receptors in some while inhibiting estrogen activity in others (the uterus) [1]. This pairing allows DUAVEE to offer estrogen efficacy in treating moderate-to-severe hot flashes and preventing postmenopausal osteoporosis while providing an alternative way to help protect the uterine lining from hyperplasia [1].

DUAVEE should not be used in women who: have or had blood clots; are allergic to any of its ingredients; have unusual vaginal bleeding; have or had certain cancers (e.g. uterine

or breast), liver problems, or bleeding disorders; or are pregnant, may become pregnant or are breastfeeding a baby [1].

### **DUAVEE Clinical Trial Program**

The approval is based on Phase III clinical trials in the Selective Estrogens, Menopause, And Response to Therapy (SMART) program. These trials evaluated the safety and efficacy of DUAVEE in generally healthy, postmenopausal women with a uterus for the treatment of moderate-to-severe hot flashes, and the prevention of postmenopausal osteoporosis [1].

Results from one trial demonstrated that DUAVEE significantly reduced the number of moderate-to-severe hot flashes by 74% at 12 weeks, as compared with placebo (47%). This means that prior to starting treatment, women on DUAVEE had on average 10 hot flashes per day while women on placebo had 11. After 12 weeks of treatment, women taking DUAVEE experienced on average three hot flashes per day while women taking placebo had six. In addition, significant decreases in mean hot flash severity were seen at 12 weeks (39%), as compared with placebo (13%) [1].

In other clinical trials, at years one and two, DUAVEE significantly increased bone mineral density in the total hip and lumbar spine from baseline compared with decreases seen with placebo [1].

Some common side effects of DUAVEE include muscle spasms, nausea, diarrhea, upset stomach, abdominal pain, throat pain, dizziness and neck pain [1]. Estrogen agonist/antagonists (including bazedoxifene) and estrogens individually are known to increase the risk of venous thromboembolism (VTE), otherwise known as blood clots [1]. Patients should talk regularly with their healthcare providers about how long to stay on treatment with DUAVEE [1].

Given that menstruation does not occur after menopause, clinicians are mindful of any vaginal bleeding that may occur in patients they are treating [4]. In women treated with DUAVEE, the rates of vaginal bleeding and spotting were evaluated and were similar to placebo [1].

### **FDA Action**

The FDA has also issued a Complete Response Letter (CRL) regarding a 0.625mg / 20mg dose of DUAVEE. This was the only dose submitted for a proposed additional indication for vulvar and vaginal atrophy (VVA).

DUAVEE was developed by Wyeth Pharmaceuticals, a wholly-owned subsidiary of Pfizer, and is part of a broader research collaboration with Ligand Pharmaceuticals Incorporated.

## **About Menopause**

Menopause is a normal, natural event. It marks the permanent end of fertility and is usually confirmed when a woman has not menstruated for 12 consecutive months [7]. Menopause is associated with reduced functioning of the ovaries due to aging, resulting in lower levels of estrogens and other hormones [7]. Changes in these hormones cause symptoms of menopause, which may include hot flashes [1] and bone loss [4]. While menopause is natural, many women have not discussed treatment options for their symptoms with their doctor [6].

“Millions of women suffer from menopausal symptoms, despite the availability of effective hormone therapies,” said Risa Kagan, MD, FACOG, Clinical Professor, Obstetrics and Gynecology, University of California San Francisco and East Bay Physicians Medical Group. “DUAVEE is an excellent option for symptomatic menopausal women who have a uterus. I’m excited to be able to offer this new, novel approach to treating moderate-to-severe menopausal vasomotor symptoms for the many women who could benefit.”

## **About Osteoporosis**

Osteoporosis, the most common bone disease in humans, becomes a serious health threat in postmenopausal women [4]. Lower levels of estrogens at the time of menopause are associated with rapid bone loss, and an increased risk of osteoporosis [4]. Approximately 50 percent of women in the U.S. 50 years of age or older have low bone mass, putting them at risk for osteoporosis [9].

## **IMPORTANT SAFETY INFORMATION**

Do not take additional estrogens, progestins, or estrogen agonists/antagonists while taking DUAVEE.

Using estrogen may increase your chance of getting cancer of the uterus. Report any unusual vaginal bleeding right away while taking DUAVEE. Vaginal bleeding after menopause may be a warning sign of cancer of the uterus. A healthcare provider should check unusual vaginal bleeding to find the cause.

Do not use estrogens to prevent heart disease, heart attacks, strokes or dementia.

Estrogens may increase the chance of getting blood clots or strokes.

Using estrogens may increase the chance of getting dementia, based on a study of women 65 years of age or older.

DUAVEE should not be used in women who: have or had blood clots; are allergic to any of its ingredients; have unusual vaginal bleeding; have or had certain cancers (e.g. uterine or breast), liver problems, or bleeding disorders; or are pregnant, may become pregnant or are breastfeeding a baby.

The use of estrogen-alone has been reported to result in an increase in abnormal mammograms requiring further evaluation. The effect of treatment with DUAVEE on the risk of breast and ovarian cancer is unknown.

Estrogens increase the risk of gallbladder disease. Discontinue estrogen if loss of vision, severe hypertriglyceridemia or cholestatic jaundice occurs.

The most common side effects include muscle spasms, nausea, diarrhea, upset stomach, abdominal pain, throat pain, dizziness, and neck pain.

## **INDICATIONS**

DUAVEE is used after menopause for women with a uterus, to reduce moderate to severe hot flashes and to help reduce the chances of developing osteoporosis.

If using or considering using DUAVEE only to prevent osteoporosis due to menopause, talk to a health care professional about whether a different treatment or medicine without estrogens might be more appropriate. Use DUAVEE for the shortest duration consistent with treatment goals and risks for the individual woman. Postmenopausal women should be re-evaluated periodically as clinically appropriate to determine if treatment is still necessary.

Please see full prescribing information, including boxed warning on [www.pfizer.com](http://www.pfizer.com).

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**PFIZER DISCLOSURE NOTICE:** The information contained in this release is as of October 3, 2013. Pfizer assumes no obligation to update forward-looking statements contained in this release as the result of new information or future events or developments.

This release contains forward-looking information that involves substantial risks and uncertainties about DUAVEE. Such risks and uncertainties include, among other things, the uncertainty regarding when DUAVEE will be available in the U.S.; uncertainty regarding the commercial success of DUAVEE in the U.S.; whether and when regulatory authorities in markets other than the U.S. will approve any applications that have been or may be filed for DUAVEE as well as their decisions regarding labeling and other matters that could affect its availability or commercial potential; and competitive developments.

A further description of risks and uncertainties can be found in Pfizer's Annual Report on Form 10-K/A for the fiscal year ended December 31, 2012 and in its reports on Form 10-Q and Form 8-K.

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#### Annotations

1 Pfizer DOF. Duavee USPI Sept. 2013.

2 Kharode Y, Bodine P, Miller C, Lyttle R, Komm B. The pairing of a selective estrogen receptor modulator, bazedoxifene, with conjugated estrogens as a new paradigm for the treatment of menopausal symptoms and osteoporosis prevention. *Endocrinology*. 2008;149:6084-6091

3 Howden L and Meyer J. Age and Sex Composition: 2010. 2010 US Census Briefs. United States Census Bureau. 2011. 1-15.

4 The North American Menopause Society. *Menopause Practice: A Clinician's Guide*. 4th Edition. 4th Ed. Mayfield, OH: NAMS; 2010.

5 Data on file. Pfizer Inc, New York, NY. [U.S. National Health and Wellness Survey. Kantar Health, 2011.]

6 The Endocrine Society. Lake Research. New Survey: Majority of women suffering menopausal symptoms are not receiving treatment; many not talking to doctors about treatment options. 2012.

7 Weismiller D. Menopause. Prim Care Clin Office Pract. 2009;36:199-226

8 Crabtree J, Peano B, Zhang X, Komm B, Winneker R, Harris H. Activity of three selective estrogen receptor modulators on hormone-dependent responses in the mouse uterus and mammary gland. Mol Cell Endocrinol. 2008;287:40-46.

9 Looker A, Melton L, Harris T, Borrud L, Shepher J. Prevalence and trends in low femur bone density among older US adults: NHANES 2005-2006 compared with NHANES III. J Bone Miner Res. 2010;25(1):64-71

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