LISA*

Osphena®
(ospemifene) tablets
60 mg

OSPHENA® COULD BE THE TREATMENT YOUR POSTMENOPAUSAL PATIENTS HAVE BEEN WAITING FOR

*Not actual patient.

Osphena® treats the most common bothersome symptoms of vulvar and vaginal atrophy (VVA) due to menopause.[1,2]

Osphena® (ospemifene) is indicated for:[1]

- the treatment of moderate to severe dyspareunia, a symptom of vulvar and vaginal atrophy, due to menopause.
- the treatment of moderate to severe vaginal dryness, a symptom of vulvar and vaginal atrophy, due to menopause.

WARNING: ENDOMETRIAL CANCER and CARDIOVASCULAR DISORDERS

Endometrial Cancer

OSPHENA is an estrogen agonist/antagonist with tissue selective effects. In the endometrium, OSPHENA has estrogen agonistic effects. There is a potential increased risk of endometrial cancer in a woman with a uterus who uses unopposed estrogens. Adequate diagnostic measures, including directed and random endometrial sampling when indicated, should be undertaken to rule out malignancy in postmenopausal women with undiagnosed persistent or recurring abnormal genital bleeding.

Cardiovascular Disorders

In clinical trials for OSPHENA (duration of treatment up to 15 months), the incidence rates of thromboembolic and hemorrhagic stroke were 1.13 and 3.39 per thousand women years, respectively, in the OSPHENA 60 mg treatment group and 3.15 and 0 with placebo. The incidence of DVT was 2.26 per thousand women years (2 reported cases) in the OSPHENA 60 mg treatment group and 3.15 per thousand women years (1 reported case) with placebo. OSPHENA should be prescribed for the shortest duration consistent with treatment goals and risks for the individual woman.

There is a reported increased risk of stroke and deep vein thrombosis (DVT) in postmenopausal women (50 to 79 years of age) who received daily oral conjugated estrogens (CE) (0.625 mg)-alone therapy over 7.1 years as part of the Women's Health Initiative (WHI).

Please see detailed Important Safety Information, including **Boxed Warning**, throughout, and accompanying Full Prescribing Information.

TREATING YOUR PATIENTS' VAGINAL SYMPTOMS

Osphena® (ospemifene) tablets 60 mg

Vulvar and vaginal atrophy (VVA) is a chronic medical condition. If left untreated, symptoms such as vaginal dryness and dyspareunia—the two most common bothersome symptoms of VVA—will not go away and may even worsen.[1–3]

Chronic conditions require long-term therapies that patients can adhere to.

Barriers to treatment adherence include:[2,4,5]

- Concerns about exposure to hormones (estrogen)
- Inconvenience of creams, inserts, rings, etc., that may stain undergarments and/or interfere with sexual spontaneity
- Discomfort with vaginal application

Up to 88% of women admitted to incorrectly using topical vaginal products (such as vaginal creams) **"on and off."**[5]

55% expressed a **preference for an oral product** instead of a topical one.[2]

"I just want something that's easy to use and gets rid of my symptoms!"†

– LISA*

MEET LISA:* A BUSY, ACTIVE WOMAN WITH PERSISTENT, DISRUPTIVE VVA SYMPTOMS

54 YEARS OLD; POSTMENOPAUSAL

Medical considerations

- Diagnosed with moderate to severe vaginal dryness, a symptom of VVA due to menopause
- Most bothersome symptoms: Discomfort while walking and biking; intermittent burning sensations
- Having persistent discomfort despite topical treatment

Personal considerations

- Dislikes the mess of vaginal cream therapy
- Tends to forget to apply her vaginal cream therapy
- Afraid to use hormones due to breast cancer in her family

*Hypothetical patient case; for illustration purposes only.
†Fictional patient quote.

FIVE REASONS TO OFFER OSPHENA® TO PATIENTS LIKE LISA

Osphena® is the first and only treatment for moderate to severe vaginal dryness and/or dyspareunia that:[1,6]

- **is non-hormonal,**
- **is an oral tablet, and**
- **acts locally‡,[1,6] (increases superficial cells, decreases parabasal cells and reduces vaginal pH).**

Important Safety Information:

Common side effects may include hot flashes, vaginal discharge, muscle spasms, hyperhidrosis, night sweats, headaches and vaginal hemorrhage. Osphena® should be prescribed for the shortest duration consistent with treatment goals and risks for the individual woman.[1]

1 OSPHENA®'S SAFETY HAS BEEN CONFIRMED BY MULTIPLE CLINICAL TRIALS[1,7]

Osphena® has the largest-studied population of postmenopausal women with vaginal dryness and/or dyspareunia, with 10 Phase 2/3 clinical trials (n=2,209) and long-term data up to 52 weeks (n=847) with no cases of endometrial cancer.

2 OSPHENA® HAS PROVEN EFFICACY[1,7,8]

Osphena® has been shown to significantly improve the condition of vaginal tissue in 12 weeks or less ($p<0.0001$ for the primary endpoint at 12 weeks; secondary endpoints were 4 and 8 weeks).

- Some patients saw improvement of the most bothersome symptom, vaginal dryness, as early as Week 4 (secondary endpoint).

3 OSPHENA® IS A NON-HORMONAL TREATMENT[1,8]

Osphena® is not a hormone. It is a selective estrogen receptor modulator (SERM) whose biological actions are mediated through the activation of estrogenic pathways in some tissues (agonism) and blockade of estrogenic pathways in others (antagonism).

4 OSPHENA® IS EASY TO TAKE[1]

Osphena® is a 60 mg oral tablet to be taken once daily with food.

5 OSPHENA® ACTS LOCALLY‡[1,6,9]

Osphena® has a strong agonistic effect on vaginal tissue while exhibiting antagonistic or mild agonistic effects on other tissues.

Please see detailed Important Safety Information, including the **Boxed Warning** regarding Endometrial Cancer and Cardiovascular Disorders, on front and back covers, and accompanying Full Prescribing Information.

‡Administered orally, distributed systemically, but active locally as a function of its characteristic tissue selectivity. Osphena® is differentiated by its agonistic activity in vaginal tissue.[6,8]

Tablet shown not actual size

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(ospemifene) tablets
60 mg

Indication and Important Safety Information including Boxed Warning

INDICATION:

OSPHENA (ospemifene) is indicated for:

- The treatment of moderate to severe dyspareunia, a symptom of vulvar and vaginal atrophy, due to menopause.
- The treatment of moderate to severe vaginal dryness, a symptom of vulvar and vaginal atrophy, due to menopause.

Important Safety Information for OSPHENA

WARNING: ENDOMETRIAL CANCER and CARDIOVASCULAR DISORDERS

Endometrial Cancer

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Cardiovascular Disorders

In clinical trials for OSPHENA (duration of treatment up to 15 months), the incidence rates of thromboembolic and hemorrhagic stroke were 1.13 and 3.39 per thousand women years, respectively, in the OSPHENA 60 mg treatment group and 3.15 and 0 with placebo. The incidence of DVT was 2.26 per thousand women years (2 reported cases) in the OSPHENA 60 mg treatment group and 3.15 per thousand women years (1 reported case) with placebo. OSPHENA should be prescribed for the shortest duration consistent with treatment goals and risks for the individual woman.

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CONTRAINDICATIONS

- Undiagnosed abnormal genital bleeding
- Known or suspected estrogen-dependent neoplasia
- Active deep vein thrombosis (DVT), pulmonary embolism (PE), or a history of these conditions
- Active arterial thromboembolic disease (e.g., stroke and myocardial infarction [MI]) or a history of these conditions
- Hypersensitivity (e.g., angioedema, urticaria, rash, pruritus) to OSPHENA or any of its ingredients
- OSPHENA is contraindicated in women who are or may become pregnant. OSPHENA may cause fetal harm when administered to a pregnant woman. Ospemifene was embryo-fetal lethal with labor difficulties and increased pup deaths in rats at doses below clinical exposures, and embryo-fetal lethal in rabbits at 10 times the clinical exposure based on mg/m^2. If this drug is used during pregnancy, or if a woman becomes pregnant while taking this drug, she should be apprised of the potential hazard to a fetus.

WARNINGS AND PRECAUTIONS

Cardiovascular Disorders

In the clinical trials for OSPHENA (duration of treatment up to 15 months), the incidence rates of thromboembolic and hemorrhagic stroke were 1.13 and 3.39 per thousand women years respectively in OSPHENA 60 mg treatment group and 3.15 and 0 per thousand women years in placebo. Should thromboembolic or hemorrhagic stroke occur or be suspected, OSPHENA should be discontinued immediately.

In the OSPHENA clinical trials, two cases of myocardial infarctions (MI) occurred in women receiving 60 mg of ospemifene.

In the OSPHENA clinical trials, two cases of DVT occurred in women receiving OSPHENA 60 mg. Should a VTE occur or be suspected, OSPHENA should be discontinued immediately.

If feasible, OSPHENA should be discontinued at least 4 to 6 weeks before surgery of the type associated with an increased risk of thromboembolism or during periods of prolonged immobilization.

Malignant Neoplasms

OSPHENA is an estrogen agonist/antagonist with tissue selective effects. In the endometrium, OSPHENA has agonistic effects. In the OSPHENA clinical trials (60 mg treatment group), no cases of endometrial cancer were seen with exposure up to 52 weeks. There was a single case of simple hyperplasia without atypia. Endometrial thickening equal to 5 mm or greater was seen in the OSPHENA up to 52 weeks treatment groups at a rate of 101.4 per thousand women vs. 20.9 per thousand women for placebo. The incidence of any type of proliferative (weakly plus active plus disordered) endometrium was 26.3 per thousand women in the OSPHENA up to 52 weeks treatment groups vs. 0 per thousand women for placebo. Uterine polyps occurred at an incidence of 19.6 per thousand women in the OSPHENA up to 52 weeks treatment groups vs. 8.3 per thousand women for placebo.

An increased risk of endometrial cancer has been reported with the use of unopposed estrogen therapy in a woman with a uterus. The greatest risk appears to be associated with prolonged use and estrogen dose. Adding a progestin to postmenopausal estrogen therapy has been shown to reduce the risk of endometrial hyperplasia, which may be a precursor to endometrial cancer. There are, however, possible risks that may be associated with the use of progestins with estrogens compared to estrogen-alone regimens. These include an increased risk of breast cancer. The use of progestins with OSPHENA therapy was not evaluated in the clinical trials.

OSPHENA 60 mg has not been adequately studied in women with breast cancer; therefore, it should not be used in women with known or suspected breast cancer.

Severe Hepatic Impairment

OSPHENA should not be used in women with severe hepatic impairment.

In clinical trials the more commonly reported adverse reactions in ≥1 percent of patients treated with OSPHENA 60 mg compared to placebo were:

1. In 12-week, double-blind, placebo-controlled clinical trials: hot flush (6.5% vs. 2.6%), vaginal discharge (3.8% vs. 0.4%), muscle spasms (1.8% vs. 0.6%) and hyperhidrosis (1.1% vs. 0.2%).
2. In all clinical trials up to 52 weeks (safety population): headaches (2.8% vs. 2.4%), hot flush (12.2% vs. 4.2), muscle spasms (4.5% vs. 2.4%), hyperhidrosis (2.5% vs. 1.8%), night sweats (1.2% vs. 0.0%), vaginal discharge (6.00% vs. 0.6%) and vaginal hemorrhage (1.3% vs. 0.0%).

The following adverse reactions have been identified during post-approval use of ospemifene:

- Neoplasms Benign, Malignant and Unspecified (including cysts and polyps); endometrial hyperplasia, endometrial cancer
- Immune System Disorders: allergic conditions including hypersensitivity, angioedema
- Nervous System Disorders: headache
- Vascular Disorders: deep vein thrombosis, thrombosis, pulmonary embolism
- Skin and Subcutaneous Tissue Disorders: rash, rash erythematous, rash generalized, pruritus, urticaria

Drug interactions: OSPHENA is primarily metabolized by CYP3A4 and CYP2C9. CYP2C19 and other pathways contribute to the metabolism of ospemifene. Do not use estrogens or estrogen agonists/antagonists, fluconazole, ketoconazole or rifampin concomitantly with OSPHENA. Co-administration of OSPHENA with drugs that inhibit CYP3A4 and CYP2C9 may increase the risk of OSPHENA-related adverse reactions. OSPHENA is highly protein-bound. Use cautiously with highly protein-bound drugs as use with other highly protein-bound drugs may lead to increased exposure of that drug or ospemifene.

Please see Full Prescribing Information for OSPHENA (ospemifene) tablets, including **Boxed Warning** and Patient Information at osphena.com/hcp.

References: 1. Osphena Prescribing Information. January 2019. **2.** Kingsberg SA, Wysocki S, Magnus L, et al. Vulvar and vaginal atrophy in postmenopausal women: findings from the REVIVE (REal Women's VIews of Treatment Options for Menopausal Vaginal ChangEs) survey. *J Sex Med*. 2013;10:1790–1799. **3.** North American Menopause Society. Management of symptomatic vulvovaginal atrophy 2013 position statement of the North American Menopause Society. *Menopause*. 2013;20(9):888–902. **4.** MacBride MB, Rhodes DJ, Shuster LT. Vulvovaginal atrophy. *Mayo Clin Proc*. 2010;85(1):87–94. **5.** Kingsberg SA, Krychman M, et al. The Women's EMPOWER Survey: Identifying Women's Perceptions on Vulvar and Vaginal Atrophy and its Treatment. *J Sex Med*. 2017;14:413–424. **6.** Simon JA, Davis SR, Althof SE, et al. Sexual well-being after menopause: an International Menopause Society White Paper. *Climacteric*. 2018;21(5):415–427. **7.** Data on file. Duchesnay USA Inc. **8.** Archer DF, et al. Efficacy and safety of ospemifene in postmenopausal women with moderate-to-severe vaginal dryness: a phase 3, randomized, double-blind, placebo-controlled, multicenter trial. *Menopause*. 2019;26(6):1–11. **9.** Archer DF, Carr BR, Pinkerton JV, et al. Effects of ospemifene on the female reproductive and urinary tracts: translation from preclinical models into clinical evidence. *Menopause*. 2015;22(7):1–11.

Visit OSPHENA.COM/HCP for more information.

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