Drug Monograph

Drug/Drug Class:	**Osphena® (ospemifeme) Tablet / Selective Estrogen Receptor Modulator**
Prepared for:	MO HealthNet
Prepared by:	Xerox Heritage, LLC

☒ **New Criteria** ☐ **Revision of Existing Criteria**

Executive Summary

Purpose:	The purpose of this monograph is to provide a review of new therapy to determine whether the reviewed drug should be made available on an open access basis to prescribers, require a clinical edit or require prior authorization for use.
Dosage Forms & Manufacturer:	Osphena® is available as a 60mg tablet which contains 60mg of ospemifeme. Shinogi Inc. Florham Park, NJ 07932 Penn Pharmaceutical Services Ltd. Tredegar, Gwent, South Wales NP22 3AA United Kingdom
Summary of Findings:	Osphena is a selective estrogen receptor modulator that has demonstrated efficacy for the treatment of moderate to severe dyspareunia.
Status Recommendation:	☐ Prior Authorization (PA) Required ☒ Open Access ☐ Fiscal Edit ☐ PDL Product
Type of PA Criteria:	☐ Increased Risk of ADE ☒ No PA Required ☐ Appropriate Indications ☐ 15 Day First Fill Fiscal Edit

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Purpose

The purpose of this monograph is to provide a review of new therapy to determine whether the reviewed drug should be considered a prior authorization drug, a clinical edit drug or an open access drug. While prescription expenditures are increasing at double-digit rates, payors are evaluating ways to control these costs by influencing prescriber behavior and guide appropriate medication usage. This review will assist in the achievement of qualitative and economic goals related to health care resource utilization. Restricting the use of certain medications can reduce costs by requiring documentation of appropriate indications for use, and where appropriate, encourage the use of less expensive agents within a drug class.

Introduction

Dyspareunia is a condition associated with declining levels of estrogen hormones during menopause. Osphena has demonstrated estrogen agonistic effects on vaginal tissue to reduce pain during sexual intercourse and also caused endometrial thickening during clinical trials. Health care professionals should monitor patients and evaluate any undiagnosed persistent or recurring abnormal genital bleeding as a potential sign of endometrial hyperplasia and/or cancer.

Dosage Form(s) [1]

Osphena® is available as a 60mg tablet which contains 60mg of ospemifeme.

Manufacturer

Shinogi Inc. Florham Park, NJ 07932

Penn Pharmaceutical Services Ltd. Tredegar, Gwent, South Wales NP22 3AA United Kingdom

Indication(s) [1]

Osphena is a selective estrogen receptor modulator that has demonstrated efficacy for the treatment of moderate to severe dyspareunia.

Clinical Efficacy [1-8] (mechanism of action/pharmacology, comparative efficacy)

PHARMACOLOGY (1,2)

Osphena is an estrogen agonist/antagonist with tissue selective effects. Its biological actions are mediated through binding to estrogen receptors. This binding results in activation of estrogenic pathways in some tissues (agonism) and blockade of estrogenic pathways in others (antagonism).

PHARMACOKINETICS (1,2,7)

Osphena is >99% protein bound with a volume of distribution of 448L. It is metabolized via the hepatic enzymes CYP3A4, CYP2C9 and CYP2C19, 75% excreted in feces and has a 26 hour terminal half-life.

EFFICACY (1-8)

SUMMARY

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The approval of Osphena was primarily based upon two 12-week, randomized, double-blind, placebo-controlled, parallel-group clinical trials involving 1745 postmenopausal women with moderate to severe dyspareunia. Study results indicated that women treated with Osphena demonstrated a statistically significant improvement in dyspareunia compared with placebo. A third 52-week, randomized, double-blind, placebo-controlled clinical trial involving 426 postmenopausal women supported the long-term safety of Osphena for dyspareunia.

CONCLUSION (1)
Osphena is effective for the treatment of moderate to severe dyspareunia.

Dyspareunia Study

STUDY DESIGN	Two 12-week, randomized, double-blind, placebo-controlled, parallel-group clinical trials (n=1745).
INCLUSION CRITERIA	Trial 1 enrolled 826 postmenopausal women aged 41 to 81 years (mean, 59 years) who had <= 5% superficial cells on a vaginal smear, a vaginal pH > 5, and at least one moderate to severe vaginal symptom that was considered bothersome (vaginal dryness, dyspareunia, or vaginal irritation/itching). All women were assessed for improvement in the mean change from baseline to week 12 for the co-primary efficacy variables 1) most bothersome symptom (MBS) of vulvar and vaginal atrophy (individual moderate to severe symptom identified as most bothersome at baseline), 2) percentage of vaginal superficial and vaginal parabasal cells on a vaginal smear, 3) and vaginal pH. Following completion of 12 weeks, women with an intact uterus were allowed to enroll in a 40-week, double-blind extension study, and women without an intact uterus were allowed to enroll in a 52-week open-label extension study. Trial 2 enrolled 919 postmenopausal women aged 41 to 79 years (mean, 59 years) who had <= 5% superficial cells on a vaginal smear, a vaginal pH > 5, and either moderate to severe vaginal dryness (dryness cohort) or moderate to severe dyspareunia (dyspareunia cohort). Primary endpoints and study conduct were similar to those in Trial 1.
EXCLUSION CRITERIA	Not specified.
TREATMENT REGIMEN	Trial 1: Patients were randomized to Osphena 30 mg, Osphena 60 mg, or placebo once daily. Trial 2: Patients were randomized to Osphena 60 mg (n=463) or placebo (n=456) once daily.
RESULTS	In Trial 1 and 2, the modified intent-to-treat population who received Osphena demonstrated a statistically significant improvement from baseline in the MBS of dyspareunia when compared with placebo (Trial 1: -1.39 vs -0.89, p=0.0012; Trial 2 -1.55 vs -1.29, p < 0.0001). A statistically significant increase in the proportion of superficial cells and a decrease in the proportion of parabasal cells on a vaginal smear were also demonstrated (p < 0.0001 for both). The mean reduction in vaginal pH from baseline to week 12 was also statistically significant (p < 0.0001).
SAFETY	Adverse reactions included hot flushes, vaginal discharge, muscle spasms, genital discharge, and hyperhidrosis.

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Contraindications[1]

- Undiagnosed abnormal genital bleeding
- Known or suspected estrogen-dependent neoplasia
- Active DVT, pulmonary embolism, or a history of these conditions
- Active arterial thromboembolic disease (eg, stroke, myocardial infarction) or a history of these conditions
- Known or suspected pregnancy

Warnings and Precautions[1]

- Endometrial cancer risk is increased in a women with a uterus using unopposed estrogens; monitor and evaluate undiagnosed persistent or recurring abnormal genital bleeding.
- Stroke and DVT have been reported; pulmonary embolism is possible; risk is increased with estrogen monotherapy; discontinue if suspected.
- Known, suspected, or history of breast cancer; caution due to lack of information; should not be used.
- Severe hepatic impairment; should not be used.

Adverse Effects[1]

Most common	Osphena 60 mg (n=1242)	Placebo (n=958)
Hot flush	7.5%	2.6%
Vaginal discharge	3.8%	0.3%
Muscle spasms	3.2%	0.9%
Hyperhidrosis	1.6%	0.6%
Genital discharge	1.3%	0.1%

Drug Interactions[1]

- CYP2C9 inhibitors: fluconazole
- CYP3A4 inhibitors: ketoconazole
- Estrogens or estrogen agonists/antagonists
- Omeprazole
- Rifampin

Dosage and Administration[1]

The recommended dose is 60 mg orally once daily with food.

Cost Comparisons (at commonly used dosages)

GENERIC NAME	BRAND NAME	MANUFACTURER	STRENGTH	DOSE	COST/ MONTH
Ospemifene	Osphena	Shionogi	60 mg tablets	1 tablet daily	$ 158.10

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*Wholesale Acquisition Cost (WAC)

Conclusion

Osphena is a selective estrogen receptor modulator that has demonstrated efficacy for the treatment of moderate to severe dyspareunia. Dyspareunia is a condition associated with declining levels of estrogen hormones during menopause. Osphena has demonstrated estrogen agonistic effects on vaginal tissue to reduce pain during sexual intercourse and also caused endometrial thickening during clinical trials. Health care professionals should monitor patients and evaluate any undiagnosed persistent or recurring abnormal genital bleeding as a potential sign of endometrial hyperplasia and/or cancer. Osphena should be prescribed for the shortest duration consistent with treatment goals and risks for the individual.

Recommendation

The Division recommends Open Access status for this product.

References

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Date: August 26, 2013

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