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Importance of Pharmacist Counseling to Increase Awareness of Available Treatments for Dyspareunia Among Postmenopausal Women

Vulvovaginal atrophy (VVA), a component of the genitourinary syndrome of menopause, is characterized by a range of symptoms associated with the declining levels of estrogen among postmenopausal women. These include vaginal dryness, burning, and itching; dysuria, or painful urination; recurrent urinary tract infections; and dyspareunia, or painful sexual intercourse.¹⁻³ As a result of declining estrogen levels, physiologic changes in the vulvovaginal area may lead to increased pH and loss of lubrication, elasticity, and pliability in vaginal tissue, causing dyspareunia.^{2,4} VVA symptoms, including dyspareunia, are progressive and may not resolve without effective treatment.²

DYSPAREUNIA PREVALENCE, AWARENESS, AND UNMET TREATMENT NEEDS AMONG POSTMENOPAUSAL WOMEN

The REVIVE and EMPOWER surveys evaluated the prevalence and impact of VVA symptoms, perceptions and awareness of VVA and its associated symptoms, knowledge of treatment options, frequency of unmet needs, and barriers to awareness and effective treatment.^{2,3} Of the 10,390 postmenopausal women surveyed across REVIVE (N = 8081) and EMPOWER (N = 2309), at least 1 VVA symptom was experienced by 38% and 80% of women in each survey, respectively. Among those with at least 1 VVA symptom, 44% and 59% reported experiencing dyspareunia in the REVIVE and EMPOWER surveys, respectively.^{2,3} Additionally, more than half of postmenopausal women with dyspareunia in the EMPOWER survey rated their discomfort as moderate to severe (54%).² Despite the prevalence of moderate to severe dyspareunia as a VVA symptom in postmenopausal women, these surveys also revealed that a substantial number of women were unaware of both VVA as a condition and its available treatment options, and therefore remained untreated.² In the EMPOWER survey, fewer than 40% of women surveyed were aware of VVA as a condition, and half of women with VVA symptoms had never received treatment.²

Surprisingly, only about half of women in the REVIVE (44%) and EMPOWER (56%) surveys had conversed with their health care provider (HCP) regarding their VVA symptoms.^{2,5} Barriers to this discussion were highlighted in the EMPOWER study, in which 18% of women reported that they were uncomfortable discussing their symptoms, 13% shared that they were unaware of treatment options for their symptoms, and 42% believed that VVA was a natural part of aging, with which they should live.² Importantly, failure of HCPs to initiate conversations regarding VVA during routine visits was also highlighted. For women who had talked to their HCPs

about VVA, fewer than 15% of conversations were initiated by the HCP.^{2,5} Discouragingly, HCPs mentioned to 20% of women that VVA symptoms were a normal part of aging with which they should learn to live.² Overall, the REVIVE and EMPOWER surveys have revealed the need for a better understanding of both VVA and available treatment options among patients and HCPs.

INTRAROSA® (PRASTERONE)

INTRAROSA® is a steroid indicated for the treatment of moderate to severe dyspareunia, a symptom of VVA, due to menopause.⁶ INTRAROSA® is a once-daily 6.5-mg intravaginal insert of prasterone that should be administered using the provided applicator every night at bedtime in either the lying or standing position.⁶ Although the mechanism of action of INTRAROSA® is not completely understood, prasterone is a synthetic version of an inactive endogenous steroid that is converted into androgens and estrogens.⁶

CLINICAL EFFICACY OF INTRAROSA® IN PROVIDING RELIEF FOR MODERATE TO SEVERE DYSPAREUNIA

The efficacy of INTRAROSA® was established across 4 phase 3 clinical trials in postmenopausal women who reported moderate to severe dyspareunia as their most bothersome symptom of VVA. Patients treated with INTRAROSA® achieved improvements in all FDA-designated co-primary efficacy end points, which included the physiologic markers of VVA (increased percentage of vaginal superficial cells, decreased percentage of parabasal cells, and decreased vaginal pH) and reductions in the severity score for dyspareunia.⁶⁻⁹ In a combined analysis across three 12-week clinical trials, INTRAROSA® treatment decreased the severity score of dyspareunia by an average of 48.9% compared with placebo ($P < .0001$).^{8,10-12} In a long-term open-label trial, INTRAROSA® reduced the severity of dyspareunia with a 46.7% decrease in severity score at 12 weeks and a 66.1% total decrease in severity score over the 52 weeks from start of the study ($P < .0001$).⁷

SAFETY CONSIDERATIONS WITH INTRAROSA®

Before starting INTRAROSA® treatment, pharmacists should counsel postmenopausal women regarding safety considerations, such as vaginal discharge and abnormal Pap smears.⁶ Vaginal discharge at the application site, which was attributed to melting suppository leakage, was the most frequently reported treatment-emergent adverse effect (AE) across the 12-week trials, occurring at

an average incidence of 5.7% in the INTRAROSA® treatment group.^{6-8,11,12} In the 52-week open-label clinical trial, AEs which occurred at an incidence of 2% or greater were vaginal discharge (14.2%) and abnormal findings on a Pap smear (2.1%).⁶ Patients should be advised to speak with their prescriber if they have a current or past history of breast cancer, and if they have undiagnosed abnormal genital bleeding.⁶

ROLE OF THE PHARMACIST

Pharmacists are uniquely positioned to address the unmet need for dyspareunia awareness and to counsel postmenopausal women on available treatment options for dyspareunia, including specific information regarding INTRAROSA®. Given that there often is a failure to initiate conversations around VVA in the postmenopausal population, pharmacists with an understanding of potential barriers to discussing this sensitive condition may be better equipped to initiate conversations with patients when appropriate. Encouragingly, 87% of postmenopausal women in the EMPOWER survey reported they would be likely to talk about their vaginal symptoms if their HCP initiates the conversation.²

Patients who are purchasing over-the-counter products or prescriptions at the pharmacy for the relief of dyspareunia may provide pharmacists with an opportunity to open a discussion about awareness of the condition and available treatment options. After initiating a conversation, the pharmacist can then refer the patient to her HCP for further evaluation, armed with knowledge to ask questions about treatments such as INTRAROSA®. The **TABLE** summarizes how to best identify and counsel women who may be at risk of

TABLE. PHARMACIST GUIDE TO COUNSELING POSTMENOPAUSAL WOMEN ABOUT DYSPAREUNIA^{3,13}

Identifying Women at Risk of Postmenopausal Dyspareunia

- Women aged 45 years and older
- Women purchasing over-the-counter menopausal treatments (ie, black cohosh or personal lubricants)

Initiating the Conversation Regarding Dyspareunia Awareness and Treatment Options

- Begin by inviting the patient to a private area to conduct consultation or answer questions.
- Normalize the conversation, mentioning that vaginal changes are common among postmenopausal women.
- Inform the patient that dyspareunia is progressive and symptoms are unlikely to resolve without treatment.
- Invite patient to share her experience, focusing on symptoms she is experiencing and products she has already tried.
- Refer patient back to her health care provider to continue the conversation about moderate to severe dyspareunia and potential treatment options such as INTRAROSA®.

postmenopausal dyspareunia and provides suggestions for opening a dialogue.^{3,13} Pharmacists have an important role in fostering a positive counseling environment for postmenopausal women and encouraging open discussions regarding dyspareunia and VVA symptoms.

References are available online at PharmacyTimes.com.

Indication

INTRAROSA® is a steroid indicated for the treatment of moderate to severe dyspareunia, a symptom of vulvar and vaginal atrophy, due to menopause.

Important Safety Information

INTRAROSA® is contraindicated in women with undiagnosed abnormal genital bleeding.

Estrogen is a metabolite of prasterone. Use of exogenous estrogen is contraindicated in women with a known or suspected history of breast cancer. INTRAROSA® has not been studied in women with a history of breast cancer.

In four 12-week randomized, placebo-controlled clinical trials, the most common adverse reaction with an incidence ≥ 2 percent was vaginal discharge. In one 52-week open-label clinical trial, the most common adverse reactions with an incidence ≥ 2 percent were vaginal discharge and abnormal Pap smear.

To report SUSPECTED ADVERSE REACTIONS, contact AMAG Pharmaceuticals at 1-877-411-2510 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see the Brief Summary of Prescribing Information on the following page. Please consult full Prescribing Information for complete product information.

PP-INR-US-00439



INTRAROSA® (prasterone) vaginal inserts

Brief Summary: Consult full Prescribing Information for complete product information.

INDICATION

INTRAROSA is a steroid indicated for the treatment of moderate to severe dyspareunia, a symptom of vulvar and vaginal atrophy, due to menopause.

CONTRAINDICATIONS

Undiagnosed abnormal genital bleeding: Any postmenopausal woman with undiagnosed, persistent or recurring genital bleeding should be evaluated to determine the cause of the bleeding before consideration of treatment with INTRAROSA.

WARNINGS AND PRECAUTIONS Current or Past History of Breast Cancer

Estrogen is a metabolite of prasterone. Use of exogenous estrogen is contraindicated in women with a known or suspected history of breast cancer. INTRAROSA has not been studied in women with a history of breast cancer.

ADVERSE REACTIONS Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

In four (4) placebo-controlled, 12-week clinical trials [91% - White Caucasian non-Hispanic women, 7% - Black or African American women, and 2% - "Other" women, average age 58.8 years of age (range 40 to 80 years of age)], vaginal discharge is the most frequently reported treatment-emergent adverse reaction in the INTRAROSA treatment group with an incidence of ≥ 2 percent and greater than reported in the placebo treatment group. There were 38 cases in 665 participating postmenopausal women (5.71 percent) in the INTRAROSA treatment group compared to 17 cases in 464 participating postmenopausal women (3.66 percent) in the placebo treatment group.

In a 52-week non-comparative clinical trial [92% - White Caucasian non-Hispanic women, 6% - Black or African American women, and 2% - "Other" women, average age 57.9 years of age (range 43 to 75 years of age)], vaginal discharge and abnormal Pap smear at 52 weeks were the most frequently reported treatment-emergent adverse reaction in women receiving INTRAROSA with an incidence of ≥ 2 percent. There were 74 cases of vaginal discharge (14.2 percent) and 11 cases of abnormal Pap smear (2.1 percent) in 521 participating postmenopausal women. The eleven (11) cases of abnormal Pap smear at 52 weeks include one (1) case of low-grade squamous intraepithelial lesion (LSIL), and ten (10) cases of atypical squamous cells of undetermined significance (ASCUS).



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