Gynecological Endocrinology

ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/igye20

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To cite this article: Faustino R. Pérez-López, Nancy Phillips, Pedro Vieira-Baptista, Bina Cohen-Sacher, Susana C. A. V. Fialho & Colleen K. Stockdale (2021): Management of postmenopausal vulvovaginal atrophy: recommendations of the International Society for the Study of Vulvovaginal Disease, Gynecological Endocrinology, DOI: 10.1080/09513590.2021.1943346

To link to this article: https://doi.org/10.1080/09513590.2021.1943346

Published online: 25 Jun 2021.

GYNECOLOGICAL ENDOCRINOLOGY
https://doi.org/10.1080/09513590.2021.1943346

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POSITION STATEMENT

Management of postmenopausal vulvovaginal atrophy: recommendations of the International Society for the Study of Vulvovaginal Disease

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ABSTRACT

Objective: To develop a best practice document for the management of postmenopausal vulvovaginal atrophy (VVA).

Method: Literature review carried out using clinical terms, treatments or interventions and comorbidity related to VVA.

Results: There is a wide variety of interventions that may produce temporal benefits for VVA. However, there are significant limitations in scientific publications concerning VVA and related issues, including variable outcome evaluations, variability in population age range, and small, often underpowered sample sizes. Therapeutic management of VVA should follow a sequential order, considering women's age, symptoms, general health as well as treatment preference. Beneficial options include lubricants, moisturizers, vaginal estrogens (estradiol, estriol, promestriene, conjugated estrogens), androgens, prasterone, and laser application. In women with general menopausal symptoms who are candidates for systemic hormone therapy, the lowest effective dose should be used. Oral ospemifene is an effective selective estrogen receptor modulator to treat VVA. Systemic androgens have a limited role. Although laser procedures are commonly used, at this moment the International Society for the Study of Vulvovaginal Disease does not endorse its use out of the setting of clinical trials. Pelvic floor muscle training improves blood flow and elasticity of the vulvovaginal tissue. In breast cancer survivors, moisturizers and lubricants are first line therapy. However, limited absorption of low/ultra-low doses of estrogens suggests safety, especially in women under treatment with aromatase inhibitors. As clinical practice and available preparations vary between countries this text should be adapted to local circumstances.

Conclusions: There is a wide range of therapeutic options to individualize VVA treatments.

ARTICLE HISTORY
Received 26 May 2021
Revised 10 June 2021
Accepted 11 June 2021
Published online 25 June 2021

KEYWORDS
Vulvovaginal atrophy; estriol; estrogens; prasterone; androgens; SERMs; ospemifene; vaginal moisturizers; lubricants; laser; breast cancer

Introduction

The vaginal wall has estrogen, progesterone and androgen receptors [1–3]. During the reproductive years, the female genital tract maintains its trophism under the stimulus of both estrogens and progesterone. After menopause the entire genital tract becomes atrophic. Androgens also play a significant role, directly and indirectly (aromatization to estrogens), in the trophism of the lower genital tract [1,4,5]. Vulvovaginal atrophy (VVA) is the most prevalent menopause-related clinical entity, continuously worsening if untreated. It is associated with dryness, dyspareunia, sexual dysfunction, nocturia, dysuria, recurrent urinary infection, and reduction of quality of life [6]. The severity of symptoms is related with the time elapsed since menopause and **the** frequency of sexual rapport. Surgical menopause or pelvic irradiation produce more severe symptoms in women during reproductive years due to the abrupt steroid decline. Many women attempt to relieve symptoms with over-the-counter products (moisturizers and/or lubricants), while others **refer** to a gynecologist or other health care professional**s** [7]. The treatment depends on symptoms, age, overall health, presence of other climacteric symptoms, and health risks.

Vaginal estrogen therapy

Vaginal estrogens are effective for the management of VVA. Several formulations are available: creams, pessaries, tablets and releasing rings. Available options include promestriene, estradiol, conjugated estrogens, and estriol [8]. The absorption is variable, depending on the degree of VVA, but plasma estrogen levels do not exceed normal postmenopausal range ($\leq$20 pg/mL) [7–9]. Topical vaginal estrogens are started with nightly application for 2–3 weeks and tapered to 2–3 times per week. However, **application** must be tailored to each woman. Creams and gels are popular, providing dosing flexibility. The estrogen releasing vaginal ring has action for 3 months, improving adherence. In some

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women with vaginal prolapse, retention of the ring may be difficult. Promestriene (estradiol 3-propyl 17β-methyl diether), a synthetic estrogen which is used vaginally in a 1% cream formulation, seems to have only intramucosal effects and has been tested in women with gynecological cancer [10,11]. Despite promising results, larger and longer series regarding long-term safety are lacking.

Ultra-low dose concentration of estriol, formulated as a vaginal gel application (1 gram containing 30 µg of estriol) significantly improves both the Vaginal Maturation Index (VMI) and pH, when compared to placebo, after 12 weeks. It also improved signs of VVA **and** adverse events were similar in both groups [12]. Vaginal tablets of estriol combined with a probiotic are also available [13,14]. Few studies **have** addressed the safety of the use of ultra-low doses of estriol in women with a history of breast cancer, showing that despite an initial peak the systemic levels remain within normal postmenopausal range [15]. Diedrich et al. [16] studied the effect of vaginal estrogens on the microcirculation architecture, density and capillary tortuosity in women with and without VVA. In the former, it is less dense and devoid of capillary loops, which can be restored by topical estrogens.

A Cochrane systematic review evaluated randomized clinical trials (RCTs) comparing vaginal estrogens versus placebo for more than 12 weeks for the management of VVA [9]. The authors concluded that there were no substantial differences regarding the effects of the different options. However, endometrial thickness was increased in women who received estrogen cream, compared to those who used rings – probably due to **the** higher dose exposure in the former. There were no differences in this aspect between tablets or cream users. A double-blind RCT in postmenopausal women with VVA showed that at 12 weeks, the VMI and pH significantly and similarly improved in women treated with estriol 0.2 and 0.03 mg, when compared to placebo. Adverse events were rare and similar in all three groups [17]. Liu et al. [18] analyzed the use of two doses of estradiol softgel (4 and 10 µg) which were shown to rapidly dissolve, be effective, and **have** minimal systemic absorption.

Biehl et al. [19] published a systematic review of 53 RCT reporting on the efficacy and safety of different vaginal estrogens used for the genitourinary syndrome of menopause. Compared to placebo, all vaginal estrogens, independently of dosages and formulations, were superior in both objective and subjective endpoints. It also showed superiority over lubricants and moisturizers for the improvement of objective, but not subjective clinical endpoints. Doses as low as 4 µg were shown to be effective [19]. Another systematic review of 20 RCTs on the use of isolated vaginal estrogen for 12–52 weeks in postmenopausal women, showed the rate of endometrial cancer and hyperplasia to be of 0.03 and 0.4%, respectively [20]. Limited available studies indicate no clear endometrial proliferation although systematic endometrial biopsies were not performed [21]. In a review of studies of one year of vaginal estrogen treatment the rate of complications was: vulvovaginal mycosis (0.73%), vaginal bleeding (0.75%), endometrial hyperplasia (0.06%) and one case of endometrial cancer (in >4500 women) [19]. Long-term follow-up studies on endometrial safety are not available. Mild transient candidiasis is common, usually not requiring treatment [22]. Finally, vaginal estrogen treatment in women not exposed to systemic menopause hormone therapy for greater than 18 years showed the risk of cardiovascular disease, cancer, and hip fracture to be similar to that of non-users of vaginal estrogen [23].

Vaginal androgen therapy

The labia majora, labia minora, vulvar vestibule, vestibular glands, vaginal mucosa, clitoris and urethra are dependent of androgens for optimal function. In the vagina it suppresses the inflammatory response of the smooth muscle cells [1] and is essential in regulating arousal and lubrication, modulating nociception and mucin secretion [1,5].

Vaginal prasterone

Dehydroepiandrosterone (DHEA; prasterone) is converted to estradiol and testosterone in the vaginal epithelium. It is administered vaginally at a daily dose of 6.5 mg with no reported risks of cancer; although no long-term studies are available. Compared to placebo, vaginal prasterone for 12 weeks was associated with improvement in dyspareunia, pH, and vaginal maturation **and** there were no endometrial changes [24]. Vaginal dryness and secretions, epithelial surface thickness and color improved, while circulating steroid levels remained within the normal range for postmenopausal women [25]. Combined results from three RCTs of postmenopausal women self-reporting moderate to severe dyspareunia as the most bothersome symptom, showed a decrease in vaginal parabasal cells (mean 35%), pH (mean 0.72), vaginal dryness and dyspareunia scores [4]. Male partners reported a positive evaluation of their sexual partners [26]. The improvement in dyspareunia and VVA with the use of prasterone was confirmed in a meta-analysis [27].

Vaginal testosterone

Intravaginal testosterone has been studied in short-term interventions (4–12 weeks). The systemic absorption of a single intravaginal dose of 2 mg in a double-blind, placebo-controlled crossover study in premenopausal women, resulted in supraphysiologic testosterone levels with no change in serum estradiol [28]. Fernandes et al. [29] randomized women aged 40–70 to receive one of these vaginal treatments: conjugated estrogens, testosterone proprionate, or placebo (glycerin lubricant) applied three times a week for 12 weeks. Hormone treatments reduced the pH to <5 and increased the vaginal cell score and the number of lactobacilli. Analyses of serum hormone levels at 6 and 12 weeks showed no significant differences between treatment and placebo groups **with** no changes in endometrial thickness **observed** in **any of the** groups [29].

A meta-analysis concluded that the effect of vaginal testosterone on sexual function and sexuality scores were similar **than** that of estrogen therapy. In breast cancer survivors taking aromatase inhibitors, sexual interest, sexual dysfunction and satisfaction had **better** improvement in the group receiving testosterone compared to the group receiving estrogens [27]. However, dyspareunia or vaginal dryness was not assessed. Longer and larger studies are needed to assess safety and efficacy [30].

Vaginal lubricants and moisturizers

Although less effective than hormone treatments, some women and physicians prefer non-hormonal therapies (moisturizers and lubricants) as first therapeutic approach to alleviate vulvovaginal symptoms related with menopause. When these are the option, preference should be given to those that have a pH and osmolality similar to those of the vagina [31].

Lubricants can be used before sexual intercourse to reduce friction and discomfort during penetrative sexual activity. Water, silicone, mineral oil, or plant-based products are applied to the vagina and vulva (if needed **these are** also **applied** to the partner's genital). In general, water soluble lubricants are associated with fewer genital side effects than silicone lubricants [31,32]. A single-center randomized double blind and crossover trial in postmenopausal breast cancer patients compared silicone- versus water-based lubricants for sexual discomfort [33]. Both showed global improvement in sexual discomfort, but pain/discomfort improved more with **the use of** silicone-based lubricants. In addition, almost twice as many women preferred this option.

Moisturizers adhere to the vaginal mucosa, promoting rehydration and mimicking **normal** lubrication. These products maintain tissue integrity, elasticity, and pliability. They should be used regularly (daily to every three days, depending on the severity of the condition). Moisturizers contain water and other substances such as hyaluronic acid or polycarbophil [31,34]. Some studies indicate that these compounds are effective in reducing symptoms of VVA, although in oncologic patients benefits may be transient. The effect of vaginal hyaluronic acid gel versus promestriene cream for 3 weeks in women with vaginal dryness was similar in one study [35].

Purified (dialyzed lyophilized) bovine colostrum, compounded as a vaginal gel, applied twice daily for 8 weeks reduced vaginal dryness, improved sexual function and the percentage of superficial cells, **that persisted** for 20 days after **treatment** interruption [34]. Vale et al. [36] studied a vaginal moisturizer composed of polycarbophil, butyl ester of a copolymer of methyl vinyl ether/copolymer, 50% sodium lactate solution, and carbopol twice a week for 12 weeks to treat vaginal dryness and sexual dysfunction. Vaginal moisture, fluid volume, elasticity and epithelial integrity improved, as well as sexual function. Participants reported being very satisfied with the treatment and product application. More than 90% of women indicated that the product did not leak nor stick to the vaginal mucosa. No severe adverse events were reported [36].

Vaginal laser

Laser **application has** produced controversial opinions due to marketing and use outside the cleared or approved intended uses. The two major types of laser are the microablative fractional carbon dioxide (CO_2) laser and the non-ablative vaginal erbium:yag laser. Both allegedly induce morphological changes in the vaginal tissue, leading to alleviation of vaginal dryness and dyspareunia [37]. For CO_2 laser, it is claimed that thermal energy deposited on the vaginal wall stimulates neovascularization, promotes collagen synthesis and improves natural lubrication with a significant improvement in vaginal health [38,39]. Cruz et al. [40] compared three arms: fractional CO_2 laser, topical estriol and laser and estriol alone for 20 weeks. The combined laser and estrogen treatment showed the most significant change in the Vaginal Health Index (VHI), and both the laser only and the combined treatment displayed significant improvement in dyspareunia, burning and dryness when compared to the estrogen group (only dryness). However, this study had some limitations: it was designed to detect differences only in **the** VHI and not in other parameters [40].

The Politano et al. [41] RCT studied the effect of three sessions of intravaginal CO_2 laser treatment, 10 mg of vaginal promestriene cream 3 times/week and vaginal lubricant alone in postmenopausal women **aged more than** 50. They reported as outcomes **the** VMI, **the VHI,** and **the** Female Sexual Function Index (FSFI) at baseline and at 14 weeks. The authors found that (i) vaginal elasticity, moisture and pH improved in the laser and promestriene arms; (ii) the VHI score was higher in the laser intervention than in promestriene and lubricant treatments; (iii) the VMI improved in both treatment arms, being more significant with laser; and (iv) there were no significant differences in FSFI total scores [41]. The VELVET multicenter RCT compared fractional CO_2 laser **with** estrogen cream in women with VVA symptoms [42]. Sixty-two women completed the six month follow-up. **The study** showed laser treatment not to be inferior to vaginal estrogens: visual analog scale scores, vulvovaginal and urinary symptoms, and sexual function did not differ between arms. VMI scores were higher in the estrogens arm. The subjective global impression and the degree of satisfaction for both interventions were statistically similar [42].

The non-ablative vaginal erbium laser maintains the postmenopausal vagina mucosa intact without causing bruising or burning [43,44]. This laser procedure has been compared to vaginal treatment with estriol, showing more pronounced improvement of clinical symptoms, maturation value, and reduction of pH up to one year after treatment. This study also documented histological favorable changes in the laser treated women. However, there are no RCTs comparing laser with vaginal hormone treatment.

Several reviews and meta-analyses on laser use for **the** management of VVA and urinary symptoms, note **that** scientific data is insufficient to demonstrate efficacy and safety, as an alternative to hormone treatments [27,45]. On the other hand, the worsening of pain following CO_2 laser application is concerning [40]. There is a need for studies including objective measurable standardized outcomes and follow-up concerning both short- and long-term consequences [46]. Currently, the International Society for the Study of Vulvovaginal Disease **(ISSVD)** does not endorse the use of these technologies out of the setting of clinical trials [45,46].

Systemic hormone treatments

Systemic MHT may be indicated for prevention or treatment of different symptoms or risks related with menopause [47]. Women receiving MHT are less likely to have VVA and sexual-related conditions. Good clinical judgment is key for the selection of appropriate pharmacological systemic treatment or intervention. The use of systemic MHT among cancer survivors or those with other chronic diseases (e.g. obesity, metabolic syndrome, hypertension, etc.), should weigh benefits against risks. In the absence of indication or if **there is** contraindication to MHT, vaginal estrogens are considered gold standard to treat VVA [48].

Menopause hormone therapy

Systemic menopause hormone therapy may be useful to control both systemic climacteric symptoms (vasomotor symptoms, sleep disturbance, nocturia) and vulvovaginal symptoms in peri- and young postmenopausal women, without contraindications. This is the case for estrogens (oral, transdermal or vaginal pessaries) alone or combined with a progestin in women with intact uterus. Transdermal application (patches, gel and spray) is also welcomed by many women, allowing self-administration. These options usually quickly restore the characteristics of the vaginal epithelium, decrease the pH and increase lubrication [30,47,49].

The lowest effective dose of MHT is recommended in order to avoid possible stimulation of the endometrium and breast tissue. The duration of MHT should be **established** on an individual basis, considering the risk of various diseases and the presence of systemic symptoms. With changing needs or risk profiles, or if vulvovaginal symptoms improve, MHT can be interrupted or changed to vaginal therapy. Results from the combination of 17β-estradiol and progesterone in a single capsule initially designed for continuous daily use to treat moderate to severe vasomotor symptoms may also prevent VVA [50].

Selective estrogen receptor modulators

Selective estrogen receptor modulators (SERMs) have different clinical effects on VVA. Tamoxifen and arzoxifene do not improve vaginal symptoms. Bazedoxifene associated with oral conjugated equine estrogens improves VVA. However, most of the effect may be related **to the** equine estrogens. The only SERM shown to improve the VMI, pH and VVA related dyspareunia is ospemifene [51]. It seems to be more effective than lubricants in the management of dyspareunia and moderate to severe VVA in postmenopausal women [52]. A meta-analysis of RCTs reporting objective outcomes and the perception of symptoms after 12 and 52 weeks of treatment with 60 mg/day of ospemifene showed a significant reduction of vaginal pH and dyspareunia and a significant improvement of vaginal maturation [53]. Hot flushes and urinary tract infections are the most commonly reported side effects at 12 weeks [54], but were not significant at 52 weeks. Ospemifene treatment was associated with significantly greater endometrial thickness at 12 and 52 weeks. Due to the short duration of the treatment, endometrial and breast cancer incidence, and metabolic changes could not be evaluated [55].

Systemic androgens

Limited data suggest that systemic testosterone may improve vaginal epithelium health and blood flow. Testosterone has been used to manage symptoms related to gonadal hormone deficiency and has anti-proliferative effects on the breast, inhibiting the stimulatory effects of estrogens. A 24-week RCT of surgically menopausal women evaluating transdermal testosterone for the treatment of hypoactive sexual desire disorder (HSDD) showed an increase in sexually satisfying events and in the arousal, but vaginal evaluation was not performed [56]. Physiologic increase in vaginal blood flow, without accompanying subjective increased arousal, has been shown for oral testosterone [57]. The transdermal use of a testosterone patch (300 µg/day) in surgically menopausal women showed no severe adverse events over a 4-year period. Local skin reactions, acne and unwanted hair growth were reported side effects. These women also received oral or transdermal estrogens and although an increase in both desire and sexually satisfying events **were** seen, no vaginal evaluation was available [58,59].

Systemic DHEA administration does not improve quality of life and is associated with androgenic side effects (mainly acne). There were no differences observed on sexual function with DHEA treatment as compared to conventional MHT [60].

Pelvic floor rehabilitation

Pelvic floor muscle training significantly reduces VVA in postmenopausal women. Mercier et al. [61] demonstrated that a 12-week program taught and monitored by physiotherapists increases vaginal wall lubrication, thickens the vaginal epithelial surface, and improves vaginal color. The improvement of VVA signs and urinary symptoms may be related to improved blood flow in the arteries supplying vulvovaginal tissues, improved pelvic floor muscle relaxation capacity, and increased vulvovaginal tissue elasticity [62].

Vulvovaginal atrophy in breast cancer survivors

Women diagnosed with breast cancer may suffer early menopause or aggravation of symptoms in those already postmenopausal, due to chemotherapy, radiotherapy and/or endocrine treatments. Menopause symptoms and the sexual dysfunction in these women are often neglected. In breast cancer survivors, estrogens are usually avoided as they may impose risk of cancer recurrence, possible interference with tamoxifen or aromatase inhibitors, or the fear of medical litigation. In general, **for** the management of VVA in breast cancer survivors, non-hormonal strategies (moisturizers or lubricants) are considered the first line.

A pH-balanced gel containing lactic acid (pH 4–7.2), applied three times per week for 12 weeks, was compared to a placebo in breast cancer survivors. It improved vaginal dryness, reduced pH and increased the VMI [63]. Hyaluronic acid and a vaginal lubricant and dilator have been studied in a sample of 49 women treated with aromatase inhibitor, showing some benefit in sexual distress and **an** increase in total FSFI score**s** [64].

Vaginal estrogens in breast cancer survivors

A meta-analysis reported the safety of vaginal estrogen application in women with breast cancer receiving aromatase inhibitors [65]. There were no changes in serum LH and estradiol **levels** while FSH almost doubled compared with baseline levels. Apparently, vaginal estrogen use was not associated with significant absorption, which may provide indirect evidence of safety. One study showed no benefit of topical vaginal estrogen in women receiving an aromatase inhibitor [66]; however, another study showed efficacy of the estradiol ring (7.5 µg/d) when compared to testosterone [67].

A RCT evaluated the efficacy and safety of an ultra-low dose of vaginal gel estriol (0.005%), as compared to placebo in women treated with aromatase inhibitor [68]. The treatment group **displayed** improved VMI, pH, dryness, global scores of symptoms and exploratory signs, as well as of FSFI **scores.** In addition, serum estrogen, LH and FSH levels remained unchanged; despite a transient negligible absorption of estriol [68]. A combined ultra-low dose of estriol with *L. acidophilus* in women with breast cancer **treated with** aromatase inhibitors showed improvement in both subjective (dryness, soreness, and dyspareunia) and objective (improved microflora and pH) markers of VVA [69]. Caution must be **taken during** the prescription of hormone treatments in patients with hormone-dependent cancers since transient elevations of estradiol have been reported in women with breast cancer under aromatase inhibitors who **received** vaginal estradiol or testosterone [70,71]. Ospemifene may be of less concern to many oncologists; however, safety data in these women is lacking. The possible influence of sporadic hormone

increases on the risk of cancer recurrence **is still not clear.** Initiation of these treatments should include discussion and consultation with both the patient and her oncologist. The regulations on the prescription of this treatment in breast cancer patients are different in European countries and the United States.

Vaginal androgens in breast cancer survivors

Open label studies have shown that high doses of intravaginal testosterone, in the presence of aromatase inhibitor, produce supraphysiologic serum testosterone levels, lowers vaginal pH, improves VMI, and reduces dyspareunia [30,67,72]. Vaginal testosterone cream was compared to estradiol vaginal rings for vaginal dryness or decreased libido in women with early-stage breast cancer treated with aromatase inhibitor. The testosterone group had better outcomes in terms of sexual function without increasing serum estradiol [67]. Despite the latter, women receiving **an** aromatase inhibitor have variable estrogen levels, especially among those presumed to be postmenopausal. This situation is critical to understand the impact of vaginal steroid hormone use for VVA. In addition, reported circulating estradiol levels **may vary depending on** the used measuring method [73].

A RCT studied vaginal prasterone at two different doses (3.25 and 6.5 mg/day), in comparison with **a** moisturizer to treat dryness and dyspareunia in postmenopausal women with breast or genital cancer receiving endocrine therapy [74,75]. All arms **displayed** improvement of FSFI **scores**. Blood DHEA levels increased in a dose-dependent **manner** while serum estradiol was increased only in those in the 6.5 mg prasterone arm. However, sex steroid levels remained within the lowest quartile for postmenopausal women [74]. Further studies are needed to document the long-term effects of this treatment.

Laser treatment in cancer survivors

Vaginal fractional CO_2 laser treatment has been evaluated in breast cancer survivors with dyspareunia and/or vaginal dryness. The majority of women were receiving aromatase inhibitors and no patient was excluded from the study due to adverse events. The visual analog scale, Urinary Distress Index, and FSFI scores were significantly improved [76].

Scientific limitations

We found significant limitations in publications concerning VVA and related issues, including heterogeneity of reported outcomes that **do** not allow comparisons or meta-analyses, which emphasizes the need for establishing core outcome settings. The evaluation of outcomes is often selective rather than comprehensive. Also, available evidence is based on short duration interventions and reduced samples. Another relevant issue is that **ages of** studied population correspond to young postmenopausal women, and VVA is a progressive phenomenon. **In this sense, there is a need for** specific information **related to** treatments in women **aged above 65.** Finally, the sexual needs and practices change with aging, and partner capabilities should also be considered in future studies.

Final remarks

Therapeutic management of VVA should follow a sequential order, considering **women's** age, symptoms and general health as well as previous treatment and patient preference. This will contribute to compliance and adhesion. Lifestyle, co-morbidity, and chronic diseases may also influence the election of treatment. Table 1 summarizes current treatment options to manage **VVA.** Vaginal options that produce benefits for VVA, include lubricants and moisturizers, estrogens (estradiol, estriol, promestriene) or prasterone. Although laser procedures are currently **used,** at this **moment** the ISSVD does not endorse its use out of the setting of clinical trials.

The lowest effective dose of systemic hormone therapy should be used to treat VVA and only in women with other menopausal symptoms and without contraindications. Oral ospemifene is an effective SERM to treat VVA. Systemic androgens have a limited role and are not indicated to treat VVA. Pelvic floor muscle training improves blood flow and elasticity **of the** vulvovaginal tissue. In breast cancer survivors, moisturizers and lubricants are first line therapy. Some evidence suggests that women under treatment with aromatase inhibitors might be treated with low doses of vaginal estriol, and experts believe **that** the receptor-blocking action of tamoxifen may improve safety of estrogen therapies.

Follow-up **of** therapeutic interventions should be individualized, and treatments should be monitored at appropriate intervals. As clinical practice and available preparations may vary

Table 1. Recommendations to manage vulvovaginal atrophy.

Treatment	Recommendation
1. Low dose and the ultralow dose vaginal estrogens.	Estradiol, conjugated equine estrogens, estriol, and promestriene are effective for VVA, and without risk of endometrial or systemic effects.
2. Vaginal prasterone	Intravaginal prasterone reduces vaginal pH, improves VMI, and decreases dyspareunia. Circulating levels of DHEA and its metabolites (testosterone and estradiol) remain in the postmenopausal range in up to 52 weeks of use.
3. Vaginal testosterone	Topical testosterone reduces vaginal pH and improves VMI and the number of lactobacilli. Longer and larger studies are needed to assess safety and efficacy.
4. Lubricants and moisturizers	Lubricants and moisturizers are appropriate for those women that cannot use or do not want to receive hormone treatments.
5. Vaginal laser	CO_2 and erbium laser treatments have been reported in women with VVA, although there is no clear evidence of the benefits as compared to hormone treatments. Currently, the ISSVD does not endorse the use of these technologies out of the setting of clinical trials.
6. Systemic hormone treatment	In young women with menopausal symptoms and without contraindications, systemic menopause hormone treatments improve VVA and related complaints.
7. Ospemifene	Oral ospemifene treatment reduces vaginal pH, improves the VMI and decreases dyspareunia. An increased rate of hot flushes may occur with initiation of treatment, but is not significant at 52 weeks.
8. Pelvic floor rehabilitation	Preliminary results suggest that pelvic floor rehabilitation may improve VVA and urinary symptoms.
9. Breast cancer survivors	In breast cancer survivors, moisturizers and lubricants are first line therapy. However, the limited absorption of low and ultra-low doses of estrogens for short period of treatment may be also considered. In this population, long term efficacy and safety data for vaginal androgens, and ospemifene are not available. Shared decision making and consultation with oncology is recommended.

from country to country this text should be adapted to local circumstances.

Acknowledgements

The authors thank the **ISSVD** Executive Council for their helpful comments.

Disclosure statement

The other authors have declared they have no conflicts of interest.

Provenance and peer review

This is a Position Statement of the ISSVD.

Funding

PVB received travel and speaker fees from Seegene® and Roche®. No funding was sought or secured for this Position Statement.

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