Vaginal Atrophy and Female Sexual Dysfunction Treatment Chart

During peri-menopause and menopause, vaginal atrophy and sexual dysfunction are often reported as problematic. Untreated vaginal atrophy can lead to painful sex and low desire. We recognize that sexual dysfunction can be caused by other causes, and a thorough evaluation needs to be done to determine if hormones or other therapies may be of benefit. Currently, there are not any FDA approved treatments for women for sexual dysfunction. Treating vaginal atrophy can include both hormone and hormone free treatment options. The chart lists active ingredients that can be used to treat vaginal atrophy and sexual dysfunction. Some information listed is anecdotal, however worthy of mention.

Testosterone, dehydroepiandrosterone and sildenafil have been studied in women for sexual dysfunction; however there are no products currently on the market for women. Often compounds for sexual dysfunction will contain several actives, designed to increase nitric oxide for vasodilation in genital tissue. Many over-the-counter products designed for women contain menthol, niacin or arginine. As compounds, many practitioners will add niacin or arginine to topical creams containing sildenafil and/or testosterone. This is a guide designed to deliver information to help with therapy decisions.

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Toni Ann Goldberg, PharmD Candidate 2013
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<tr>
<th>Drug</th>
<th>Mechanism of Action</th>
<th>Dosing</th>
<th>Notes</th>
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<tr>
<td>Menthol USP</td>
<td>Vasoconstrictor; tingling cooling effect</td>
<td>Up to 0.025 % topical use 0.16%</td>
<td>May burn or cause genital irritation; do not apply to broken or irritated skin</td>
<td>No studies found</td>
</tr>
<tr>
<td>Niacin (nicotinic acid)</td>
<td>Vasoconstrictor</td>
<td>Up to 2 % topical</td>
<td>No studies found</td>
<td></td>
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<tr>
<td>Peppermint oil</td>
<td>High menthol content Cooling effect, tingling</td>
<td>0.1 mL/100 grams</td>
<td>The amount used should be small percent, and consider amount being applied.</td>
<td>No studies found</td>
</tr>
<tr>
<td>Vitamin E acetate</td>
<td>Anti-inflammatory, antioxidant, skin/wound healing</td>
<td>200 – 400 iu/day oral</td>
<td>No literature for monotherapy; could use 100 iu-400 iu intravaginal as a cream</td>
<td>No studies found</td>
</tr>
<tr>
<td>Vitamin A palmitate</td>
<td>Increases function of immune local cells and integrity of vaginal epithelium</td>
<td>1 mg/intra-vaginal dose</td>
<td>Combination therapy</td>
<td>Costantino D, Guaraldi C. Effectiveness and safety of vaginal suppositories for the treatment of the vaginal atrophy in postmenopausal women; an open, non-controlled clinical trial. <em>Eur Rev Med Pharmacol Sci.</em> 2008 Nov-Dec;12(6):411-6</td>
</tr>
<tr>
<td>Sodium hyaluronate</td>
<td>Moisturizer; maintains water balance aiding in skin elasticity</td>
<td>5 mg intra-vaginally every other day x 2 weeks, then twice weekly</td>
<td>30 participants experienced reduced symptoms &amp; increase incidence of superficial and intermediate cells after treatment for 90 days.</td>
<td>Karaosmanoglu O, Cogendez E, Sozen H, et al. Hyaluronic acid in the treatment of postmenopausal women with atrophic vaginitis. <em>Int J Gynaecol Obstet.</em> 2011 May;113(2):156-7. Epub 2011 Mar 21</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5mg per ovule (combination with vitamin A &amp; E QHS x 2 weeks, then every other day)</td>
<td>130 women reported significant improvement in vaginal itching, burning, irritation and dyspareunia. Total 4 weeks</td>
<td>Costantino D, Guaraldi C. Effectiveness and safety of vaginal suppositories for the treatment of the vaginal atrophy in postmenopausal women; an open, non-controlled clinical trial. <em>Eur Rev Med Pharmacol Sci.</em> 2008 Nov-Dec;12(6):411-6</td>
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Estrogen

Acts locally to increase secretions, decrease vaginal pH and prevent urogenital infections; stimulates cell proliferation of vaginal mucosa and lower urinary tract

10μg and 25μg vaginal tablets

230 women included. Both doses provided relief (25μg showed greater benefit) of vaginal symptoms & increased vaginal and urethral maturation.


10μg 17β-estradiol vaginal tablet

309 women studied. Treatment effect on vaginal cytology and maturation seen after 2 weeks. Symptom relief apparent after 4 weeks.


12.5μg micronized estradiol vaginal tablet twice weekly for 12 weeks

In 8 breast cancer survivors, provided improvement in vaginal symptoms and sexual function with insignificant change in serum estrogen levels.


1gm cream containing 0.625mg conjugated equine estrogens +/- 0.5gm 0.2% testosterone cream

75 postmenopausal women experienced significant benefit in urogenital and sexual function with significant change in serum estrogen levels.


Estriol

(Estriol USP does not have an FDA approved indication)

Decreases vaginal pH → increases presence of vaginal lactobacillus thus prevention of urogenital infections; promotes cell proliferation of the vaginal mucosa

1mg vaginal ovule qd x 2 weeks, then 2 ovules once weekly for a total of 6 months

In 88 postmenopausal women, significant improvement in symptoms was seen.


1mg/day intravaginal x 21 days

In 31 postmenopausal women, all complaints improved and an increase in estrogenic level was observed.


0.03mg and 0.2mg pessaries daily x 20 days, then twice weekly for 9 weeks

438 total study subjects. Improvement comparable between doses in vaginal pH and atrophy symptoms. Greater improvement with 0.2mg dose in vaginal maturation index.


0.5mg/day vaginal cream daily x 3 weeks, then twice weekly through 4 months

In 27 early postmenopausal women, vaginal estriol improved vaginal symptoms sooner than HT alone; both evolved to show similar improvement at the end of the 4 month study.

### Estriol

**0.25mg cream twice weekly x 12 weeks**

In 10 breast cancer survivors, provided improvement in vaginal symptoms and sexual function with insignificant change in serum estrogen levels.


1gm gel containing 50µg estriol daily x 3 weeks, then twice weekly up to 12 weeks

Study of 167 women. Low-dose estriol shown to be superior to placebo in improvement of vaginal dryness.


### Estriol/Pregesterone (combination)

**1mg estriol + 30mg progesterone suppository daily x 2 weeks, then 3X/week through 6 months**

19 women with atrophic vaginitis treated an observed improvements in vaginal dryness without endometrial hyperplasia


50µg/day 17-β estradiol transdermal + 5mg/day oral medroxy-progesterone acetate plus 0.5mg/day estriol cream

In 27 early postmenopausal women, vaginal estriol improved vaginal symptoms sooner than HT alone; both evolved to show similar improvement at the end of the 4 month study.


### Alprostadil (prostaglandin E₁)

**0.05, 0.1, and 0.2% cream applied to vaginal wall in office**

Patients reported significant increases in amount of lubrication with higher doses and increased subjective arousal.


500, 1000, 1500mcg cream applied to vulvar area 5-30 min prior to anticipated sexual intercourse

94 premenopausal women with FSAD; changes indicate improvements in sexual activity and sexual distress levels, greatest benefits seen in 1000mcg dose.


100mcg or 400mcg solution applied to external genitalia in office

39 patients receiving 400mcg experienced significantly greater changes in genital warmth/tingling, level of sexual arousal, and sexual satisfaction.


500, 700, and 900mcg cream applied 5-30min prior to sexual intercourse

374 women with FSAD completed the study; treated patients observed improved sexual arousal rates.

Testosterone

Precursor for other sex hormones (DHT and estradiol)

300mcg patch twice weekly in naturally postmenopausal women on stable oral HRT

433 women included. Satisfying sexual activity seen at 4 weeks; improved desire and personal distress not seen until 8 weeks


Dosing that is consistent with levels seen in younger patients with normal menses

Testosterone administered in physiological doses by non-oral route appears safe for up to 2 years when given with exogenous estrogens


10 mg cream daily to thigh x 12 weeks

Study included 34 premenopausal women. Restored general well-being, and nearly half of women experienced a 50% improvement in sexual function score


2.2 mg/day alcoholic gel to upper arm

BLISS study, designed to evaluate long-term CV safety and risk of breast cancer. Currently enrolling and randomizing patients.


10 mg applied to thigh or abdomen

Controlled cross-over design of 131 postmenopausal cancer survivors. Estradiol-depleted patients did not see benefit in libido, pleasure, mood, or vitality in 4-weeks of treatment.


Vaginal atrophy, 1 gram dose: 150 mcg (used testosterone propionate) OR 300 mcg (used testosterone micronized) cream; Avoid use on labia majora, clitoris

In 20 women currently on AI’s, Improvement in severity of dyspareunia and vaginal dryness. No difference in symptom severity between the 150μg and 300μg doses given for 28 days.


Dehydroepiandrosterone (DHEA)

Precursor for androgens and estrogens that promote collagen formation in the vaginal epithelium, lamina propria and muscularis (proposed MOA for improvement of vaginal atrophy)

216 postmenopausal participants, marked improvements in sexual desire, arousal, orgasm, and pain during intercourse seen with 12 weeks of treatment


3.25mg 6.5mg, 13mg intravaginal ovule QHS

DHEA serum levels and metabolites measured; values remained within normal range for postmenopausal women

Labrie F, Archer D et al. Serum steroid levels during 12-week intravaginal dehydroepiandrosterone administration. Menopause. 2009 Sep-Oct;16(5):897-906
<table>
<thead>
<tr>
<th>Dehydroepiandrosterone (DHEA) continued</th>
<th>see above</th>
<th>15mg transmucosal daily</th>
<th>case report in female for libido with success</th>
<th>Dr. Johnathan Wright, Nutrition &amp; Healing Vol 15, Issue 10 December 2008</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>4g 10% DHEA cream or gel applied to thighs, or two 50mg oral caps daily before breakfast</td>
<td>DHEA is transformed into active androgens and estrogens in peripheral intracrine tissues with minimal/no release of active steroids into circulation.</td>
<td>Labrie F, Bélanger A, et al. Bioavailability and metabolism of oral and percutaneous dihydroepiandrosterone in postmenopausal women. Journal of Steroid Biochemistry &amp; Molecular Biology. 2007; 107: 57-69.</td>
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**Sildenafil**

- Proposed mechanism in females: relaxation of clitoral and vaginal smooth muscle and vasodilation allowing for improved blood flow in the genitals
- 50mg 1 hour prior to planned sexual activity, no more than once daily x 3 months
- 202 post-menopausal women; those without HSDD had significant benefit in arousal sensation, lubrication, and orgasm.
- Of 30 women treated, non-significant increase in subjective lubrication and clitoral sensation scores.


- 25-100mg x 12 weeks
- 577 estrogenized and 204 estrogen-deficient women tolerated therapy, but did not perceive improvement in sexual response including vaginal lubrication and clitoral sensation.


**Nifedipine**

- Vasodilation 0.2% topical
- No studies found

**Ergoloid mesylate**

- Proposed mechanism – vasodilation; Alpha receptor blocker, regulates smooth muscle responsiveness, may facilitate vasodilation in combination
- 0.05% topical
- 36 men studied; Significantly increased penile arterial flow and improved erectile dysfunction without producing clinically significant side effects. More effective in psychogenic than organic vascular impotence.


**Isosorbide dinitrate**

- Converts to nitric oxide → vasodilation
- 0.25 % topical
- See above

See ergoloid mesylate reference

**Aminophylline (releases theophylline)**

- Non selective phosphodiesterase inhibitor, ↑ cAMP → smooth muscle relaxation
- 3% (study); May need higher doses as anecdotally seen topical dosing 3 – 10 %

See ergoloid mesylate note

See ergoloid mesylate reference
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<th>Effect</th>
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<tr>
<td>Naltrexone</td>
<td>Counteracts the effects of endogenous opiates thought to contribute to sexual dysfunction by inhibiting gonadotropins</td>
<td>25 mg oral daily for 3 days; 25 mg oral once daily x 4 weeks, then bid x 4 weeks. Topical dose of 0.817% was shared by member pharmacist.</td>
<td>Sathe RS, Komisaruk BR, Ladas AK, Godbole SV. Naltrexone-induced augmentation of sexual response in men. <em>Arch Med Res</em>. 2001 May-Jun;32(3):221-6</td>
</tr>
<tr>
<td>Oxytocin</td>
<td>Enhances sexual arousal</td>
<td>Information below is anecdotal*; Nasal spray 8-40 IU, Vaginal/clitoral cream 10-40 u/mL. Troches or SL drops ranges 5-100 u/dose; 5-20 units every morning to increase happiness, social connectedness. For low oxytocin levels and for better orgasm, consider 50-100 units 1 hour prior to sex.</td>
<td>MacDonald K, Feifel D. Dramatic improvement in sexual function induced by intranasal oxytocin. <em>J Sex Med</em>. 2012 Mar;9:1407-10</td>
</tr>
<tr>
<td>Cyproheptadine</td>
<td>5HT-2 Antagonist may reverse the inhibiting effect of antidepressants on orgasm.</td>
<td>Consider a clitoral cream (1 - 4 mg) to prevent oral side effects. 4-12 mg orally 1-2 hr prior to sexual activity or up to 16 mg daily in divided doses. In 7 males with SRI-induced sexual dysfunction;</td>
<td>Aizenberg D, Zemishlany Z, Weizman A. Cyproheptadine treatment of sexual dysfunction induced by serotonin reuptake inhibitors. <em>Clin Neuropharmacol</em>. 1995;18(4):320-24</td>
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