



# Estrogen Vaginal Preparations

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Genitourinary syndrome of menopause (GSM) occurs with decreasing estrogen levels. Vaginal atrophy (atrophic vaginitis, a symptom of GSM) results in thinning, inflammation and dryness of the vaginal wall and can occur during perimenopause or menopause due to the lack of estrogen. The symptoms that occur due to the thinning of the vaginal tissue and subsequent involvement of the urinary tract may present as vaginal dryness, irritation, itching, burning, urgency, urinary tract infections and painful intercourse.<sup>1</sup> These symptoms can be very bothersome to a patient and can have a negative effect on the patient's quality of life. (See PCCA Document #98289 for more information on vaginal atrophy.)

## TREATMENT OPTIONS AND ISSUES

Vaginal forms of estradiol and conjugated estrogens have been available in commercial dosage forms for years. Estriol vaginal formulations are very well-known options among patients and physicians who are familiar with compounding pharmacies. But while estriol is commercially available in other countries (including the UK), in the United States, it is only available through compounding pharmacies. Therefore, patients and prescribers often request compounded vaginal preparations of estrogen in specific compounding bases for various clinical reasons. (See PCCA Document #97762 and #99172 for more information.)

Additionally, a new opportunity has recently arisen to show the clinical benefits of estriol and other compounded preparations to those who are unfamiliar with compounded options. The prices of various commercial estrogen formulations have become increasingly unaffordable for patients, who are often faced with rejections by insurance companies or extremely high copays. They are often unable to get their prescriptions filled, leading many who don't know about compounding with no choice but to search for OTC treatments that often provide minimal if any relief.

## COMMERCIAL ESTROGEN FORMULATIONS

| NAME                    | API                        | GENERIC | AVG. COST TO PHARMACY |
|-------------------------|----------------------------|---------|-----------------------|
| Premarin® Vaginal Cream | Estrogens (conjugated)     | None    | \$250/30 Gm           |
| Estrace® Cream          | Estradiol 0.01%            | None    | \$250/42.5 Gm         |
| Vagifem®                | Estradiol 10 mcg (tablets) | None    | \$381/18 tablets      |

Based on the chart to the left, there is a unique opportunity for compounding pharmacists to reach out to these patients, which can benefit a compounder's business and, most importantly, can improve patients' lives

## OPPORTUNITIES IN COMPOUNDING

In addition to our traditional compounding options, something new to consider is a lower strength of estriol than previously used in vaginal formulations. A study evaluated the efficacy of a low dose estriol with *Lactobacillus acidophilus* in the treatment of vaginal atrophy. It was used as a vaginal tablet and inserted once daily for twelve days, and then one tablet for two consecutive days each week for twelve weeks. The low dose estriol combination vaginal tablet was superior to placebo with respect in the Vaginal Maturation Index (VMI) after the daily therapy, and relapse did not occur during the weekly therapy.<sup>2</sup>

PCCA has written new formulas with low-strength estriol utilizing MucoLox™ for its superior mucoadhesive properties. An example is PCCA Formula #12124 – Estriol 0.03 mg/Gm/Acidophilus 10 MU/Gm Vaginal Gel (MucoLox/VersaBase®).

Another study showed that ultra-low concentration vaginal gel helped significantly improve the trophism (growth) of the vaginal mucosa, sexual health and quality of life. Subjects with symptoms of atrophy and sexual disorders used 50 mcg estriol gel vaginally daily for three weeks, and then twice weekly for up to twelve weeks. Patients on the estriol vaginal gel showed an increase in VMI and improvement on vaginal pH compared to baseline.<sup>3</sup>

A comparable new related formula is PCCA Formula #12123 – Estriol 0.005% Vaginal Gel (MucoLox/VersaBase).

Also noted in the literature is a study where local estriol therapy showed positive effects in patients diagnosed with vulvodynia and interstitial cystitis/bladder pain syndrome (IC/BPS). The effects of estriol 0.5 mg applied vulvo-vaginally three times per week for twelve weeks in 34 premenopausal women on sexual and urinary/bladder symptoms were examined. There were positive effects on both urinary and sexual function as well as an improvement in the Vaginal Health Index (VHI).<sup>4</sup>

## NEW HRT OPPORTUNITY FOR COMPOUNDING PHARMACIES (Continued)

Some related formulas are:

- PCCA Formula #11115  
Estriol 0.05% Vaginal Gel (MucoLox/VersaBase)
- PCCA Formula #12033  
Estriol 0.05% Vaginal Gel (MucoLox/VersaBase)
- PCCA Formula #12034  
Estriol 0.5 mg/Gm Vaginal Cream (VersaBase)
- PCCA Formula #8980  
Estriol 5 mg/mL Vaginal Cream

## OTHER VAGINAL ESTRIOL FORMULAS

- PCCA Formula #11116  
Estriol 0.1%/Testosterone 0.1% Vaginal Gel (MucoLox/VersaBase) (FormulaPlus™ ➔ BUD Study)
- PCCA Formula #12032  
Estriol 0.1%/Testosterone 0.1% Vaginal Gel (MucoLox/VersaBase)
- PCCA Formula #12031  
Estriol/Estradiol [50%/50%] 0.5 mg/0.5 Gm Vaginal Gel (MucoLox/VersaBase)
- PCCA Formula #12116  
Estriol/Estradiol [50%/50%] 0.25 mg to 1 mg/0.5 Gm Topical Cream (VersaBase) (FormulaPlus ➔ BUD Bracketed Study)

Always remember that we are just one call away if you have questions. Please contact the PCCA Pharmacy Consulting Department at 800.331.2498.

## REFERENCES

- <sup>1</sup> Rahn, D.D., Carberry, C., Mamik, M.M., Ward, R.M., Meriwether, K.V., Olivera, C.K., . . . Murphy, M. (2014). Vaginal estrogen for genitourinary syndrome of menopause: a systematic review. *Obstetrics & Gynecology*, 124(6), 1147-1156. doi:10.1097/AOG.0000000000000526
- <sup>2</sup> Jaisamrarn, U., Triratanachat, S., Chaikittisilpa, S., Grob, P., Prasauskas, V., & Taechakraichana, N. (2013). Ultra-low-dose estriol and lactobacilli in the local treatment of postmenopausal vaginal atrophy. *Climacteric*, 16(3), 347-355. doi:10.3109/13697137.2013.769097
- <sup>3</sup> Caruso, S., Cianci, S., Amore, F.F., Ventura, B., Bambili, E., Spadola, S., & Cianci, A. (2016). Quality of life and sexual function of naturally postmenopausal women on an ultralow-concentration estriol vaginal gel. *Menopause*, 23(1), 47-54. doi:10.1097/GME.0000000000000485
- <sup>4</sup> Gardella, B., Iacobone, A.D., Porru, D., Musacchi, V., Dominoni, M., Tinelli, C., . . . Nappi, R.E. (2015). Effect of local estrogen therapy (LET) on urinary and sexual symptoms in premenopausal women with interstitial cystitis/bladder pain syndrome (IC/BPS). *Gynecological Endocrinology*, 31(10), 828-832. doi:10.3109/09513590.2015.1063119

*Always make sure you have checked the PCCA Formula Database and are following the most up-to-date version of a formula as changes are continuously made to existing formulations to provide the highest quality.*

*The formulas and/or statements listed are provided for educational purposes only. They are compounding ideas that have commonly been requested by physicians, and have not been evaluated by the Food and Drug Administration. Formulas and/or material listed are not to be interpreted as a promise, guarantee or claim of therapeutic efficacy or safety. The information contained herein is not intended to replace or substitute for conventional medical care, or encourage its abandonment. Every patient is unique, and formulas should be adjusted to meet their individual needs. ©*

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