

Vaginal Estrogen therapy for genitourinary symptoms

We have noted common questions regarding use of vaginal estrogen therapy in our patients. We attach the following list of references validating the use of vaginal estrogen therapy for our patients.

Systemic absorption and side effects:

There is minimal absorption with vaginal estrogen therapy. However, when the vaginal mucosa is most atrophic is also when it is most permeable, so minor absorption may occur at the beginning of treatment until the mucosa matures and becomes less permeable. This may lead to symptoms of bloating or breast tenderness. This “spill-over effect” has been estimated to be transient over the first 7 to 14 days. The serum estradiol concentration returns to pre-treatment levels thereafter and remains low on serial assay over 12 weeks, which suggests that there is no long-term accumulation of estradiol with vaginal therapy.

Eugster-Hausmann M, Waitzinger J, Lehnick D. Minimized estradiol absorption with ultra-low-dose 10 microg 17beta-estradiol vaginal tablets. *Climacteric* 2010;13:219-227.

SOGC Guideline No. 311, September 2014 Managing Menopause. Chapter 5, Urogenital health

Cardiovascular disease:

In the Nurse’s health study, over 18 years of follow-up, including 85,941 women, risks for cardiovascular disease, cancer, and hip fracture were not different between users and nonusers of vaginal estrogen.

Vaginal estrogen use and chronic disease risk in the Nurses’ health study. *Menopause*: [June 2019 - Volume 26 - Issue 6 - p 603-610](#)

Because systemic absorption of vaginal estrogen is minimal, its use is **not** contraindicated in women with contraindications to systemic estrogen therapy (for example, history of cardiac or thromboembolic disease).

SOGC Guideline No. 311, September 2014 Managing Menopause. Chapter 5, Urogenital health

Patients who have had Breast Cancer:

The decision to use vaginal estrogen may be made in coordination with a woman’s oncologist.

ACOG Committee Opinion No 659, March 2016, reaffirmed 2020. The use of vaginal estrogen in women with a history of estrogen dependent breast cancer.

There are currently insufficient data to recommend its use in women with breast cancer who are receiving aromatase inhibitors (where the goal of adjuvant therapy is a complete absence of estrogen at the tissue level). Its use in this circumstance needs to be dictated by quality-of-life concerns after discussion of possible risks.

SOGC Guideline No. 311, September 2014 Managing Menopause. Chapter 5, Urogenital health

Endometrial cancer risk:

Large observational studies evaluating longer exposures to vaginal estrogen identified no increase in endometrial cancer. In the Women’s Health Initiative-Observational Study, the rate of endometrial cancer was not statistically different in users of vaginal ET compared with nonusers (1.3 vs 1 case per 1,000 woman-years, respectively). Thus, occurrence of endometrial cancer and hyperplasia with low-dose vaginal ET use is rare and consistent with rates in the general population.

Crandall CJ, Hovey KM, Andrews CA, et al. Breast cancer, endometrial cancer, and cardiovascular events in participants who used vaginal estrogen in the Women's Health Initiative Observational Study. *Menopause* 2018;25:11-20

Frequency of use:

Vaginal estrogen creams are generally used **two to three times weekly**, estradiol tablets and inserts used twice weekly, and the estradiol ring changed every 3 months.

North American Menopause society position statement: 2020 genitourinary syndrome of menopause. *Menopause: The Journal of The North American Menopause Society* Vol. 27, No. 9, pp. 976-992

Overall safety:

A prospective cohort study of approximately 45,000 women in the Women's Health Initiative Observational Study examined risks associated with vaginal estrogen use. Outcomes assessed included coronary heart disease (CHD), invasive breast cancer, colorectal cancer, endometrial cancer, and death.

The findings were very reassuring, with no increased risk of heart disease or cancer in postmenopausal women using vaginal estrogens.

Crandall CJ, Hovey KM, Andrews CA, et al. Breast cancer, endometrial cancer, and cardiovascular events in participants who used vaginal estrogen in the Women's Health Initiative Observational Study. *Menopause* 2018;25:11-20