



Therapeutic Class ReviewSM

Vaginal Estrogens

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Available Therapeutic Alternatives:

Preferred/Formulary	Non-preferred/Non-formulary
conjugated estrogen cream (Premarin) [Wyeth]	micronized estradiol 0.01% cream (Estrace) [Warner-Chilcott]
	estradiol ring (Estring) [Pfizer]
	17 beta-estradiol tablet (Vagifem) [Novo-Nordisk]

Executive Summary

- Vaginal estrogen products are approved for the treatment of urogenital symptoms (vaginal itching, dryness, dyspareunia, and increased incidence of urinary tract infections) associated with vaginal atrophy and/or the lower urinary tract.
- Vaginal estrogens should be prescribed at the lowest possible dose for the shortest duration of time, to treat symptoms and minimize systemic absorption
- Evaluation of pharmacokinetic trials is uncertain.
 - Studies used inconsistent units for reporting serum estrogen levels, which can potentially lead to misinterpretation of evidence reported in clinical trials.
 - Each study has multiple methodology flaws including small sample size, open-label design, and significant loss to follow up
 - All products appear to have an initial systemic estradiol burst within the first 15 days of continuous therapy. It decreases once vaginal mucosa has been restored, though it is unclear whether this burst is clinically significant.
- Specific vaginal estrogen products have been promoted for differences in systemic estrogen absorption and pharmacokinetic properties. Analysis of available data is inconclusive.
- A Cochrane Review identified several limitations to vaginal estrogen trials. Evidence is insufficient to determine differences in safety and efficacy among products. Given these limitations, Cochrane concluded that:

- Creams, tablets, and the estradiol vaginal ring appeared equally effective in relieving the symptoms of vaginal atrophy.
- Women favored the estradiol vaginal ring for ease of use, comfort of product, and overall satisfaction.
- Evidence should be interpreted with caution due to small trial numbers and significant variability among results.
- Obstetricians and gynecologists report similar comments regarding vaginal estrogen products. Vagifem and Estring are more widely favored among patients, primarily due to convenience.

Conclusion:

Vagifem is a formulary/preferred product because:

- It provides another option for our members.
- It provides good clinical value relative to its cost.

References:

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