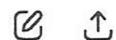


notelovitz et al and first study of vagifem 10 vs 25 mg dosages

Here's a summary of the **Notelovitz et al. study** and the **first comparative research of Vagifem 10 µg vs 25 µg** (both are low-dose estradiol vaginal tablets used for menopausal atrophic vaginitis):

Notelovitz et al. — Vagifem 10 vs 25 µg (12-week study)



twice weekly for the remaining 10 weeks in postmenopausal women. LWW +1

- **Population:** Healthy postmenopausal women with vaginal atrophy and low baseline serum estradiol. LWW
- **Primary outcomes:**
 - Both doses **improved vaginal maturation index (VMI)**, lowered vaginal pH, and relieved symptoms of atrophic vaginitis (dryness, irritation). PMC +1
 - The **25 µg dose tended to show greater improvements** in symptom relief and biological markers than the 10 µg dose. LWW
 - A significant proportion of women in both groups had increased vaginal epithelial maturation after 12 weeks. PMC
- **Systemic absorption:** Both doses had **minimal systemic estradiol absorption**, with the 10 µg dose producing lower serum levels than the 25 µg dose. PMC
- **Safety:** There was **no significant systemic effect**, and neither dose was associated with appreciable increases in systemic estradiol in most women. Endometrial effects were minimal. PMC

Background and context

- Estradiol vaginal tablets like **Vagifem** are indicated for treating **atrophic vaginitis due to menopause** by restoring estrogen effect locally in the vaginal mucosa. FDA Access Data
- The **25 µg formulation** was the original marketed dose; later the **10 µg ultra-low dose formulation** was approved to allow effective local therapy with even lower systemic absorption and risk. PR Newswire +1

- FDA approval and clinical reviews confirm both doses **improve symptoms and vaginal cytology**, but historically **the 25 µg dose showed larger effects** in some endpoints.

Medscape

Key Takeaways

- **Notelovitz et al.** provided pivotal data comparing **10 µg vs 25 µg Vagifem**, showing both doses effective at improving signs of vaginal atrophy over ~12 weeks. LWW
- The **higher 25 µg dose generally produced greater improvements** in clinical and cytological measures compared with the 10 µg dose, although both were beneficial.

LWW

- Systemic absorption with either dose is low, minimizing broader hormonal effects while targeting local vaginal tissues. PMC

Notelovitz research on low dose Vagifem vaginal tablets

Here's a clear, research-focused summary of **Morris Notelovitz's work and related clinical research on low-dose Vagifem (estradiol vaginal tablets)** — especially as it relates to treatment of atrophic vaginitis in postmenopausal women. Rutgers University +1

Key Research on Low-Dose Estradiol Vaginal Tablets (Vagifem)

1. Notelovitz *et al.* — Efficacy of Low-Dose Vaginal Estradiol Tablets

- A multicenter, randomized, double-blind, placebo-controlled clinical trial evaluated 10 mcg and 25 mcg estradiol vaginal tablets versus placebo in 230 postmenopausal women with symptoms of atrophic vaginitis. Rutgers University
- Both 10 mcg and 25 mcg doses significantly improved:
 - Composite vaginal symptom scores (e.g., dryness, irritation, dyspareunia)
 - Vaginal pH (lowering toward premenopausal levels)
 - Vaginal and urethral epithelial maturation — signs of healthier tissues relative to placebo. Rutgers University
- Improvement was generally **greater with 25 mcg**, but both doses were clinically effective. Rutgers University
- After the 12-week randomized period, patients could continue on 25 mcg estradiol up to 52 weeks in an open-label extension, with sustained benefits. Rutgers University

This study is widely cited as key evidence that **low-dose estradiol vaginal tablets (the basis of Vagifem) effectively relieve symptoms of urogenital atrophy** associated with menopause. Rutgers University

2. Earlier Clinical Evidence: 25 mcg Estradiol Vaginal Tablets

- A **double-blind placebo-controlled study** (published in *European Journal of Obstetrics & Gynecology and Reproductive Biology*) showed that a **25 mcg estradiol vaginal**

tablet significantly reduced vaginal atrophy symptoms compared with placebo over 12 weeks. [PubMed](#)

- Treatment also improved related urogenital symptoms such as vaginal dryness and dyspareunia. [PubMed](#)

3. Endometrial Safety of Ultra-Low-Dose (10 mcg) Vaginal Estradiol

Since safety—especially **endometrial safety** with estrogen therapies—is a major clinical concern, several large studies have looked at long-term effects of *ultra-low-dose* estradiol vaginal tablets:

- A 12-month trial with **10 mcg estradiol tablets** in **non-hysterectomized postmenopausal women** showed **no cases of endometrial hyperplasia or cancer** attributable to the treatment. Most biopsy samples remained atrophic or inactive after 52 weeks. [PubMed](#)
- A pooled analysis combining two studies of 10 mcg estradiol vaginal tablets found **very low incidence** of endometrial hyperplasia/carcinoma (< 0.6% per year), consistent with expected background incidence in this age group. [PubMed](#)

These findings support that **local low-dose vaginal estrogen has minimal systemic stimulation of the endometrium** in appropriate use conditions. [PubMed](#)

Interpretation and Clinical Context

Vagifem (estradiol vaginal tablet) historically was marketed in doses such as 10 mcg and 25 mcg to treat **atrophic vaginitis** (now often referred to as **genitourinary syndrome of menopause [GSM]**). Studies like those authored/co-authored by Notelovitz demonstrated:

- **Symptom relief:** improvement in dryness, dyspareunia, irritation.
- **Tissue health:** lowering of vaginal pH and better epithelial maturation.
- **Safety:** favorable endometrial safety profiles over up to 12 months with low doses.

[Rutgers University](#) +1

These outcomes are consistent with the clinical rationale that **local estrogen at low doses works directly on vaginal tissues with minimal systemic exposure.** [Rutgers University](#)

Bottom Line

- Research including Notelovitz and colleagues shows that **low-dose estradiol vaginal tablets (e.g., 10 mcg and 25 mcg)** significantly improve vaginal atrophy symptoms and markers of vaginal health compared with placebo. Rutgers University
- Both doses helped but **25 mcg often showed stronger effects**; the 10 mcg dose has reassuring longer-term safety data. Rutgers University +1
- Long-term use at these low doses generally **did not stimulate the endometrium** in most study participants. PubMed