

Indiana Medicaid Therapeutics Committee **Therapeutic Class Review Summary**

Therapeutic Class:

Vaginal Estrogen Preparations

Overview:

Many postmenopausal women enter a hypoestrogenic state that leads to symptoms such as vaginal dryness, dyspareunia, vaginal infections, irritation, discomfort, and even some forms of incontinence.⁸ Surveys suggest that approximately 45% of menopausal women complain of the aforementioned symptoms.¹² Topical estrogens may improve postmenopausal vaginal atrophy, vasomotor symptoms, and cervical cytologic changes.¹³ Estrogen is a generic term for any substance, natural or synthetic that exerts biological effects characteristic of estrogenic hormones.¹⁴ Estrogens occur naturally in several forms. Estradiol is the principal intracellular premenopausal human estrogen and is substantially more active than its metabolites, estrone and estriol, at the cellular level. Estrone is a naturally occurring steroidal estrogen. Estrone is one-third less active at the cellular level than estradiol. Conjugated estrogens are traditionally a mixture of the water-soluble salts of sulfate esters from estrone, equilin, 17 alpha-dihydroequilin, and other related steroids. Once estrogens enter the cells of responsive tissues, they increase the rate of synthesis of DNA, RNA, and some proteins. At the cellular level, estrogens increase cervical secretions, cause proliferation of the endometrium, and increase uterine tone.⁵ All vaginal estrogen preparations have a black box warning against the increased risk of endometrial cancer with the use of estrogen. In addition, topical estrogens should not be used for the prevention of cardiovascular disease or dementia.

Five estrogen vaginal products are currently available in the United States. Estrace[®] Vaginal Cream, Premarin[®] Vaginal Cream, and Femring[®] are indicated for the treatment of vulvar and vaginal atrophy. Vagifem[®] is indicated for atrophic vaginitis, while Femring[®] is also indicated for the treatment of vasomotor symptoms associated with menopause. Premarin Vaginal Cream was recently approved for use in the treatment of moderate to severe dyspareunia, a symptom of vulvar and vaginal atrophy, due to menopause. Ortho[™]-Dienestrol and Ogen[®] Vaginal Cream are no longer marketed in the United States. Intravaginal administration of estrogens does not seem to have adverse effects on the endometrium; however, systemic absorption of these products does occur. The clinical literature for this therapeutic class includes few studies, all with very small sample sizes. Additionally, the studies do not yield data that suggests the superiority of any product in the class.

Generic Name	Trade Name	Manufacturer	Generic
Estradiol	Estrace [®] Vaginal Cream	Warner Chilcott	N
	Estring [®]	Pharmacia	N
	Vagifem [®]	Novo Nordisk	N
Conjugated estrogens	Premarin [®] Vaginal Cream	Wyeth-Ayerst	N
Estradiol acetate	Femring [®]	Warner Chilcott	N

Summary:

There is no potential for abuse or misuse of this drug class, and the benefits of these medications will outweigh the costs. The clinical literature does not establish product superiority. Hence, current utilization, cost, and patient acceptance should determine which medications are included on the preferred drug list.