*Indian Health Service*
**IHS National Pharmacy and Therapeutics Committee**
**Estradiol**
**December 2010**

**Background:** [1-2]
Menopause is a syndrome brought on by a reduction in estrogen production in women or after surgical removal of the ovaries. It frequently presents in the early fifties with numerous vasomotor symptoms, including, flushing, sweating, sleep disturbance and mood changes. Additionally, women may experience vaginal dryness and urogenital atrophy. During this menopausal and post-menopausal period, women become at risk for the onset of osteoporosis.

**Discussion:**
Estrogen replacement is frequently utilized to help with vasomotor symptom control. Additionally, estrogen replacement has been approved by the FDA for prevention of low bone density and fracture. A progestin should be added for women with an intact uterus to avoid endometrial hypertrophy. This combination therapy may be given continuously or cyclical. The addition of a progestin may adversely affect lipid levels, and may lead to headache, bloating and breast tenderness. Thromboembolic complications (PE, stroke and CHD events) are increased for patients receiving hormone replacement therapy.[1-2]

Several products are available in this class of medications and include conjugated estrogens (Premarin®); synthetic conjugated estrogens, A (Cenestin®); synthetic conjugated estrogens, B (Enjuvia®); esterified estrogens (Menest®, Neo-estrone®); 17β-estradiol (Estrace®, various generics); estradiol acetate (Femtrace®) and estropipate (Ortho-Est®, Ogen®, various generics).[3]

A comparative effectiveness review analyzed the available clinical trial data that looked at placebo controlled and head-to-head trials of estrogen products. These data show that all studied estrogen products improved vasomotor symptoms compared to placebo. With the head-to-head trials, this evidence-based review did not identify a superior product for the improvement of vasomotor symptoms. For the prevention of low bone density and fractures, this review found that all studied products were superior to placebo, but did not identify a superior product in head-to-head trials.[1] Similarly, a Cochrane review did not identify a clinically superior product.[2]

***Dose Equivalence:**[3]

| Estradiol | Conjugated Estrogen | Esterified Estrogen | **Estropipate | Transdermal Estrogen |
|---|---|---|---|---|
| 0.5mg | 0.3mg | 0.3mg | 0.75mg | 25mcg/day |
| 1mg | 0.625mg | 0.625mg | 1.5mg | 50mcg/day |

***Note:** Women's Health Initiative recommends lowest dose to achieve desired effect.
****Note:** Ogen 0.625=0.75mg estropipate, Ogen 1.25=1.5mg estropipate, Ogen 2.5=3mg estropipate; estropipate is prepared from purified crystalline estrone

**Findings:**
The NPTC reviewed the agents used for hormone replacement (HRT) at its June 2010 meeting and during the recent HRT update at its December 2010 meeting. During the June meeting, the clinical review and analysis did not identify a clinically superior product in the oral estrogen class of medications and subsequently added the class to the National Core Formulary (NCF). Based upon this clinical information, the committee decided to look further into the pharmacoeconomic data associated with this class. Utilization data from Q4FY2010 by units purchased revealed Premarin® holding approximately 60% of the market share followed by Menest® at 23%, estradiol (generic) at 15%, Cenestin® at 1% and both Enjuvia® and estropipate (generic) at <1%, respectfully. In contrast, market share by dollars purchased revealed Premarin® holding 86% of the market share followed by Menest ® at 10% with the remaining products comprising the remaining 4% of the market. With increased utilization of estradiol, IHS can realize approximately *$1.9 million in annual cost avoidance*. Based upon the relative clinical equivalence and favorable pharmacoeconomic data, the NPTC named estradiol tablets to the NCF.

If you have any questions regarding this document, please contact the NPTC at nptc1@ihs.gov.

**References:**


**1.** Nelson HD NP, Freeman M, Chan BKS. Drug Class Review on Hormone Therapy. http://www.ohsu.edu/drugeffectiveness/reports/final.cfm. 2007.

**2.** Farquhar CM, Marjoribanks J, Lethaby A, Lamberts Q, Suckling JA. Long term hormone therapy for perimenopausal and postmenopausal women. *Cochrane Database Syst Rev.* 2005(3):CD004143.

**3.** UpToDate-Online 18.3. *http://www.uptodate.com/online/content/image.do?imageKey=ENDO%2F5364; accessed December 23, 2010.*