Drug Use Research & Management Program
Oregon State University, 500 Summer Street NE, E35, Salem, Oregon 97301-1079
Phone 503-947-5220 | **Fax** 503-947-1119

Month/Year of Review: November 2014 **Date of Last Review:** January 2014
PDL Classes: Hormone Replacement Therapy (HRT) **Source Document:** OSU College of Pharmacy

Current Status of PDL Class:

Current Preferred Agents	Current Non-Preferred Agents
Oral HRT - Estrogen	
Estradiol	Conjugated Estrogens, Synthetic B (Enjuvia®)
Conjugated Estrogens, Synthetic A	Esterified Estrogens/methyltestosterone
Estropipate	Esterified estrogens (Menest®)
	Estradiol/norethindrone (Activella®)
	Drospirenone/estradiol (Angeliq®)
	Norethindrone acetate/ethinyl estradiol (Jinteli®)
	Estradiol/norethindrone acetate (Mimvey®)
	Estradiol/norgestimate (Prefest®)
	Conjugated estrogens/Medroxyprogesterone (Prempro®, Premphase®)
	Norethindrone acetate/Ethinyl Estradiol (FEMHRT)
Topical HRT - Estrogen	
Estradiol patch (Climara)	Estradiol gel packet (Divigel®)
	Estradiol gel pump (Elestrin®)
	Estradiol patch (Estraderm®)
	Estradiol patch (Estrasorb®)
	Estradiol gel pump (EstroGel®)
	Estradiol spray (Evamist®)
	Estradiol patch (Vivelle-dot®)
	Estradiol/norethindrone acetate patch (Combipatch®)
	Estradiol/levonorgestrel patch (Climara Pro®)
Vaginal HRT - Estrogen	
Estradiol tablet	Estradiol vaginal cream (Estrace®)
Conjugated Estrogen cream	Estradiol vaginal ring (femring®)

Previous Conclusions and Recommendation:

- Evidence does not support a difference in efficacy/effectiveness
- Evidence does not support a difference in harms/adverse events
- Recommend including one or more agents from this category
- Estrogen plus progestin and estrogen alone decreased risk for fractures but increased risk for stroke, thromboembolic events, gallbladder disease, and urinary incontinence.
- Estrogen plus progestin increased risk for breast cancer and probable dementia, whereas estrogen alone decreased risk for breast cancer.
- There are insufficient data to assess the risk of long term hormone therapy use in perimenopausal women or postmenopausal women younger than 50 years of age.
- Hormone therapy for postmenopausal women with an intact uterus should comprise both estrogen and progestin to reduce the risk of endometrial hyperplasia.
- There were no consistent differences by age and comorbidities in subgroup analyses.

- Despite of lacking randomized clinical trials evidence for potential favorable thromboembolic risks using transdermal formulation of hormone therapy, several national guidelines recommended transdermal route of administration over oral route.

Research Questions:

- Is there any new comparative evidence in reducing symptoms of menopause, preventing low bone density, or preventing fractures?
- Is there any new comparative safety evidence of the different preparations?
- Are there subpopulations of patients for which one medication or preparation is more effective or associated with fewer adverse effects?

Methods:

The DERP scan was used to identify any new comparative research that has emerged since the last P&T review.[1]

Conclusions and Recommendations:

- There is high quality evidence that estrogens are the most effective agents at relieving common symptoms associated with menopause, including vasomotor symptoms and quality of life, with no significant differences between doses or mode of administration. There is high strength of evidence that vaginal estrogen reduces pain during intercourse and insufficient evidence for oral estrogen.
- There is no new significant comparative evidence on the efficacy or safety of hormone replacement therapy medications; no further review or research needed.
- Evaluate comparative costs in executive session.

Systematic Reviews:

A draft AHRQ report reviewing the evidence evaluating the comparative effectiveness of treatments for menopausal symptom relief and long term harms was available.[2] It is unknown when the final review will be completed. Menopausal symptoms that were evaluated include vasomotor symptoms, quality of life, psychological symptoms, sexual function, urogenital atrophy, and sleep dysfunction. The most commonly studied agents were estrogens, isoflavones, and SSRI/SNRIs. Overall, the authors concluded that there is good evidence available showing that estrogens are the most effective at relieving common symptoms associated with menopause, and there are no significant differences between doses or mode of administration. There is high strength of evidence that estrogen is the most effective agent in relieving vasomotor symptoms (SMD -0.7 or lower compared with placebo) and high strength of evidence that difference doses of estrogen are equally effective. There is high strength of evidence that vaginal estrogen reduces pain during intercourse compared to placebo (SMD -0.50; 95% CI -0.71 to -0.29) and insufficient evidence that oral estrogen reduces pain. Estrogens are also accompanied by other potential long-term benefits and harms that require consideration. Compared with estrogen, other agents have lesser efficacy and limited evidence on long-term benefits and harms. There is low strength evidence that estrogen alone reduces breast cancer risk. There is moderate strength evidence that estrogen has no effect on coronary heart disease and high strength of evidence that estrogen therapy increases the risk of venous thromboembolic events. There is moderate strength evidence that estrogen therapy reduces the risk of osteoporotic fractures.

References:

1. Peterson K. Drug Effectiveness Review Project: Drug Class Review on Hormone Therapy for Postmenopausal Women or Women in the Menopausal Transition Stage. Preliminary Scan Report #5. July 2014.

2. Agency for Healthcare Research and Quality. Menopausal Symptoms: Comparative Effectiveness Review of Therapies. Draft Comparative Effectiveness Review. Available at: http://effectivehealthcare.ahrq.gov/search-for-guides-reviews-and-reports/?pageaction=displayproduct&productid=1022