

# Express Scripts

## RESEARCH STUDY FINDINGS

### The Change in the Use of Hormone Replacement Therapies (HRT) Combination Products, Estrogens and Other Agents Used to Treat Osteoporosis Since the Release of HERS II and WHI Findings

By

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#### Purpose:

Findings from two studies released in July, 2002 — a follow up to the Heart and Estrogen/Progestin Replacement Study called HERS II and the Women's Health Initiative (WHI) conducted by the National Institutes of Health (NIH) — call into question the relative safety of combination estrogen/progestin hormone replacement therapy (HRT) products, particularly Premphase® and Prempro®. HERS II showed that combination HRT was not effective in preventing coronary heart disease (CHD) for older postmenopausal women with existing CHD. HERS II participants using HRT had a higher risk of blood clots than those taking placebo. The combination HRT part of the WHI was discontinued 3 years before the planned completion date after evidence accumulated that combination HRT not only did not protect against CHD, but women using it actually had higher risks of having CHD, strokes and blood clots. An unacceptably higher risk of breast cancer was also seen in WHI study participants taking HRT. Both studies were published in the Journal of the American Medical Association.

To assess physician and member reaction to these unfavorable findings, Express Scripts researchers analyzed the use of combination HRT products before and after the issuance of the HERS II and WHI information. More specifically, ESI addressed the extent to which the use of the HRT combination products Prempro and Premphase, estrogens, and other agents (such as Evista®, Fosamax® and Actonel®) that are used to treat osteoporosis changed after these highly publicized studies were released in July.

To answer these questions, a sample of 372,777 Prempro, Premphase, Premarin and other estrogens, Evista, Fosamax and Actonel users 18 or older and who were continuously eligible in the Express Scripts commercial book of business between March 10, 2002 and November 10, 2002 was selected. Utilization patterns of these users in the four month pre-period between March 10, 2002 and July 9, 2002 were compared to usage in the four month post-period from July 10, 2002 to November 10, 2002. These utilization patterns were compared to usage for a sample of 112,247 continuously eligible Prempro, Premphase, Premarin and other estrogen, Evista, Fosamax and Actonel users 18 or older in the Express Scripts commercial book of business for similar periods in 2001.

#### Major Findings:

1. The percent of members who discontinued their use of HRT combination products between the pre- and post-periods increased significantly from 8.4% in 2001 to 36.0% in 2002.
2. The proportion of combination HRT users switching to estrogens or to other agents used to treat osteoporosis between the pre- and post periods increased modestly from 1.5% in the 2001 period to 3.8% in the 2002 timeframe.
3. Although adverse effects were not found among estrogen users in the HERSII and WHI studies, the percentage of estrogen users who discontinued use of any estrogen and who did not switch to a

combination HRT product or to another agent used to treat osteoporosis more than doubled from 9.5% in 2001 to 22.6% in 2002.

4. The incidence rate (new users) among women 18 and older who used HRT combination products, estrogens and other agents used to treat osteoporosis declined from 1.6% to 1.1% between 2001 and 2002, due to the reduced number of new HRT combination product and estrogen users.
5. Of these new users the utilization of:
  - Combination HRT products decreased from 14.1% in 2001 to 6.7% in 2002
  - Estrogen products declined from 58.2% in 2001 to 51.0% in 2002
  - Other agents used to treat osteoporosis grew from 27.7% in 2001 to 42.3% in 2002.

Generally, these results suggest that many physicians and patients are alarmed enough about the HERS II and the WHI findings to have ceased using HRT combination drugs, and secondarily estrogen products, or are beginning to use non-estrogen products — Evista, Fosamax and Actonel.