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14 **STATE OF NEVADA**

**DISTRICT COURT
CLARK COUNTY, NEVADA**

16 **STATE OF NEVADA**

17 Plaintiff,
18 v.

19 **WYETH, WYETH PHARMACEUTICALS
20 INC.; PFIZER INC., and PHARMACIA &
21 UPJOHN COMPANY,**

22 Defendants.

FILED

Nov 19 1 59 PM '08

CASE NO.: **A575980**

DEPT NO.: **XII**

IN RE: HORMONE THERAPY LITIGATION
[Consolidated into *Gray v. Wyeth, et al.*,
Case# 04-A-488234 Per 11/1/06 Order]

COMPLAINT

23 Plaintiff, STATE OF NEVADA, by and through its attorneys, Attorney General
24 Catherine Cortez Masto, Peter C. Wetherall, Esq., of White & Wetherall, LLP, and Zoe
Littlepage, Esq., and Rainey Booth, Esq., of Littlepage Booth, avers and alleges as follows:

I.

INTRODUCTION

1
2
3 Plaintiff, STATE OF NEVADA, brings this action in the public interest pursuant to the
4 Nevada Deceptive Trade Practices Act, NRS 598.0903 et. seq. as well as other common
5 law claims to protect consumers, physicians and Defendants' competitors from unlawful,
6 unfair and deceptive business practices. By this action, Plaintiff seeks to obtain restitution,
7 reimbursement, forfeiture, injunctive relief, civil penalties, disgorgement of profits, treble
8 damages, reasonable attorney's fees, costs, and such other and further relief as the Court
9 deems necessary to prevent the deceptive acts and practices alleged in this complaint, and
10 to remedy the consequences of such practices.

11 II.

JURISDICTION AND VENUE

12 1. Jurisdiction over the subject matter of this action which alleges violations of
13 the Nevada Deceptive Trade Practices Act lies with this Court pursuant to Article 6, §6 of
14 the Nevada constitution, and NRS 598.0963.

15 2. Venue lies with this court pursuant to NRS 598.0989. Defendants at all times
16 material hereto, solicited consumers and business within the state of Nevada and the
17 deceptive trade practices alleged herein occurred throughout Nevada, including Clark
18 County.

19 III.

PARTIES

20
21 3. Plaintiff is the state of Nevada, represented by Catherine Cortez Masto, the
22 Attorney General, who is authorized to bring this action pursuant to NRS 598.0963, in
23 conjunction with privately retained counsel.

24 4. Defendant, Wyeth, is a Delaware corporation with a principal place of
business in New Jersey. Wyeth is licensed to do business in all states of the United States

1 of America including the State of Nevada. At all relevant times, Wyeth was engaged in the
2 design, manufacture, production, testing, study, research, inspection, mixture, labeling,
3 marketing, advertising, sales, promotion, and/or distribution of pharmaceutical products,
4 including hormone therapy drugs, including but not limited to Premarin, Cycin, Prempro
5 and Premphase for ultimate sale and/or use throughout the United States of America as
6 well as in various foreign jurisdictions.

7 5. Defendant, Wyeth Pharmaceuticals Inc., is a Delaware corporation with a
8 principal place of business in Pennsylvania. Wyeth Pharmaceuticals Inc. is licensed to do
9 business in all states of the United States of America including the State of Nevada. At all
10 relevant times, Wyeth Pharmaceuticals Inc. was engaged in the design, manufacture,
11 production, testing, study, research, inspection, mixture, labeling, marketing, advertising,
12 sales, promotion, and/or distribution of pharmaceutical products, including but not limited to
13 the hormone therapy drugs Premarin, Cycin, Prempro and Premphase for ultimate sale
14 and/or use throughout the United States of America as well as in various foreign
15 jurisdictions.

16 6. Defendant Pharmacia & Upjohn Company, is a Delaware corporation,
17 headquartered and with a principal place of business in New Jersey. At all times relevant
18 hereto, Pharmacia & Upjohn Company was engaged in, *inter alia*, the business of testing,
19 manufacturing, labeling, marketing, distributing, promoting and selling hormone therapy
20 drugs, including but not limited to Provera and medroxyprogesterone acetate ("MPA").

21 7. Defendant Pfizer Inc. is a Delaware corporation headquartered and with a
22 principal place of business in New York. At all times relevant hereto, Pfizer Inc. was
23 engaged in, *inter alia*, the business of testing, manufacturing, labeling, marketing,
24 distributing, promoting and selling hormone therapy drugs, including Provera and
medroxyprogesterone acetate ("MPA").

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- Educational materials to encourage discussion between the doctor and patient;
- Advertisements directed to physicians in medical journals and materials;
- Direct to consumers advertisements about the products;
- Promotional or advertising materials directed to the patients including pamphlets, Slim Jims, tear sheets etc.
- Sponsoring medical journal articles;
- “Ghost writing” medical journal articles that discuss HRT;
- Sponsored continuing medical education programs including lunch-and-learns, telephone conference calls, dinner meetings etc.
- Hiring experts in the field to speak to other physicians either one on one or in small group meetings;
- Sponsoring medical and pseudo-medical organizations to make statements supporting the use of the products;
- Sponsoring medical organizations’ position statements or printed pamphlets such as ACOG, NAMS etc.;
- Sponsoring booths at physician conventions;
- Writing, editing or influencing the content of lay publications such as Good Housekeeping publications;
- Labels or warnings on HRT including information published in the Physician’s Desk Reference;
- Press releases;
- Dear Health Care Provider letters;

1 11. Through these various methods of communication, Defendants knowingly,
2 intentionally and deliberately made false representations about the benefits and risks of
3 HRT in order to induce greater sales and use of HRT in the state of Nevada. Defendants
4 knowingly misrepresented the following issues:

- 5 ▪ That HRT was appropriate for all woman or “each newly diagnosed
6 menopausal patient” as opposed to a narrow and defined group of
7 menopausal women;
- 8 ▪ That HRT was appropriate for long-term use including campaigns or sales
9 objectives such as “get her on, keep her on” or “for all women for life”;
- 10 ▪ That HRT conveyed heart or cardiac benefits as well as protection against
11 the development of heart problems;
- 12 ▪ That HRT conveyed mental or cognitive benefits or helped protect against the
13 development of Alzheimer’s disease;
- 14 ▪ That HRT prevented macular degeneration, helped a woman’s hair and skin
15 and helped protected a woman’s vision;
- 16 ▪ That HRT protected a woman’s bones and provided long-term bone density
17 benefits;
- 18 ▪ That the breast cancer risk from HRT was minimal, insignificant or unknown;
- 19 ▪ That the use of estrogen (E) and progesterin (P) in combination was
20 appropriate, safe, approved and recommended;
- 21 ▪ That HRT was safe and appropriate for use in menopausal women.

22 12. In 1942, Ayerst, the predecessor to the Wyeth Defendants, received approval
23 for Premarin, which is a conjugated equine estrogen made from the urine of pregnant
24 mares. Wyeth began marketing its product as a hormone replacement product to replace
the natural female hormone estrogen. Premarin has remained chemically unchanged until

1 today. Even today Wyeth does not know all of the biologically active components of
2 Premarin.

3 13. In 1959, the Pfizer defendants received approval to market Provera,
4 medroxyprogesterone acetate, a synthetic progestin that was approved for abnormal
5 bleeding issues.

6 14. Defendants have always tried to turn the natural aging process of
7 menopause into a disease worthy of pharmaceutical manipulation. Defendants have
8 encouraged doctors and patients to consider hormone therapy drugs for all women going
9 through menopause.

10 15. In 1966, Dr. Robert Wilson published a bestseller book entitled *Feminine*
11 *Forever*. In *Feminine Forever*, Dr. Wilson recommended estrogen as the “cure” for “the
12 tragedy of menopause.” He argued that women who use the drugs “will be much more
13 pleasant to live with and will not become dull and unattractive.” In writing about the
14 menopause condition, which he termed the “deficiency disease,” Dr. Wilson wrote that
15 “aside from keeping a woman sexually attractive and potent . . . estrogen preserves the
16 strength of her bones, the glow of her skin, the gloss of her hair . . . Estrogen makes
17 women adaptable, even-tempered, and generally easy to live with.” Dr. Wilson asserted
18 that estrogen *prevented* breast and genital cancers, such as endometrial cancer (i.e.,
19 cancer of the uterine lining). Unbeknownst to readers, Dr. Wilson was financially
20 supported by Wyeth to write, publish, promote and market this book. While disguised as
21 an independent project, *Feminine Forever* was nothing more than a bestselling promotional
22 piece for Wyeth’s estrogen products. There was no reliable science to support Dr. Wilson’s
23 assertions or claimed benefits.

24 ////

1 16. Soon after the publication of Dr. Wilson's book, Wyeth's sales force began to
2 distribute the book to physicians throughout the country. Wyeth spent thousands of dollars
3 supporting Dr. Wilson's promotional book tour, and sales of Premarin increased
4 dramatically.

5 17. In 1974 and 1975, Wyeth started a round of advertising that recommended
6 Premarin as an alternative to tranquilizers for the treatment of symptomatic or mild
7 depression caused by menopause. In a print advertisement that Wyeth published in the
8 October 13, 1975 edition of *JAMA*, Wyeth claimed that "tension, irritability, headaches,
9 undue fatigue, depression and insomnia," when caused by declining menopausal estrogen
10 levels, may be relieved with Premarin. Additionally, at the top of the advertisement, in
11 large print, Wyeth advised doctors, "Almost any tranquilizer might calm her down . . . but at
12 her age, estrogen may be what she really needs." The 1975 advertisements stated: "in the
13 treatment of middle-aged depression, there may be one thing to add... Premarin." Again
14 no clinical studies or reliable science supported these representations.

15 18. In 1977, the Food & Drug Administration ("FDA") issued a statement
16 confirming that estrogen therapy should not be used to treat simple nervousness during
17 menopause and that there was no scientific support for any representation that such
18 therapy could keep a woman feeling young or her skin soft.

19 19. By the mid-70s more than 30 million prescriptions for Premarin were being
20 written every year, eventually making it the fifth most frequently prescribed drug in the
21 United States. Eventually Premarin became the most frequently dispensed prescription
22 drug in the United States. For many years, Premarin was the most profitable drug for the
23 Wyeth Defendants and Provera was "number 1 in terms of profitability" for the Pfizer
24 Defendants.

1 20. In 1975, the first hormone therapy health epidemic was brought to light. In
2 the New England Journal of Medicine ("NEJM") in 1975, two articles appeared that linked
3 estrogen therapy to a significantly increased risk of women developing endometrial cancer.
4 Quickly physicians stopped prescribing Premarin for women with intact uteri.

5 21. To counteract these declining sales, it quickly became popular to prescribe
6 estrogen (Premarin) with progestin (Provera). The Premarin was designed to alleviate a
7 woman's menopausal symptoms while the Provera would provide no actual additional
8 benefit but merely protect her from developing endometrial cancer. From the late 1970s
9 on, a common combination prescription was the use of Premarin with Provera (E+P).
10 Defendants never told doctors or patients that this combination use was not approved by
11 the Food & Drug Administration (FDA). In addition, Defendants never warned doctors and
12 patients that the use of E+P had not been subjected to any long-term studies and that the
13 adverse effects of these drugs were unknown and untested.

14 22. In the 1980s, Defendants added a new spin to the marketing of hormone
15 therapy drugs by claiming that HRT could help prevent bone loss. Defendants informed
16 women that osteoporosis is a devastating disease and that HRT could treat it.

17 23. Defendants also sought to claim that HRT could prevent or reduce
18 cardiovascular disease. Indeed, Defendants' sales representatives encouraged doctors to
19 prescribe HRT even if a woman was not having menopausal symptoms because of the
20 therapy's purported cardiac benefits.

21 24. Defendants consistently scared women about a wide variety of purported
22 illnesses and ailments associated with menopause. Among other things, Defendants
23 represented that loss of natural hormones causes bones to become brittle, skin to become
24 dry, and sexual intercourse to become painful and irritating. At the same time Defendants

1 minimized or downplayed any dangers and risks associated with HRT. Defendants
2 represented that HRT provided "long term health protection" and should be continued
3 indefinitely, even after short-term menopausal symptoms, such as hot flashes, had
4 subsided.

5 25. In 1994, Wyeth got approval for its next marketing blockbuster: combination
6 hormone therapy in a single pill. Wyeth's product, Prempro is an oral medication that
7 combines Premarin and synthetic progestin in a single pill taken one time per day. A
8 similar Wyeth product containing the same combination of compounds is brand named
9 Premphase. Premphase delivers both CEE and MPA for only part of the monthly regime
10 and then CEE alone without the MPA component for the rest of the month. Wyeth now
11 had multiple hormone therapies in the "Premarin family of products" to market and
12 promote.

13 26. Soon after introduction of Prempro, Wyeth agreed to fund a four-year heart
14 disease prevention trial, called HERS: Heart and Estrogen/Progestin Replacement Study.
15 Wyeth touted the study as one that would show that Prempro prevented heart disease in
16 women who were at high risk for heart disease. Wyeth was seeking FDA approval of the
17 use of Prempro to prevent or reduce the risk of heart disease. But in 1998, the HERS
18 investigators reported that hormone therapy did not reduce the rate of coronary heart
19 disease events in women with heart disease and in fact dramatically increased the risk of
20 heart disease and heart attack in those women, especially in the first year. The HERS
21 results were immediately minimized or ignored by Wyeth and its sales representatives.

22 27. With no actual science to support its assertions, Defendants continued
23 inappropriately marketing HRT to doctors and patients. Beginning in early 1999, Wyeth
24 even distributed a brochure to women through the waiting rooms of physicians' offices, that

1 claimed, "Menopause isn't gone in a flash — its debilitating consequences can affect the
2 rest of your life." The Body of Evidence promotional campaign also directed women to
3 "Take a few minutes to think about the rest of your life" and listed a number of conditions
4 which neither Prempro nor Premarin had been approved by the FDA to treat, including
5 Alzheimer's disease, vision problems, tooth loss, heart disease, and colon cancer.

6 28. In a magazine advertisement that featured model Lauren Hutton, Wyeth
7 made a rash of similar claims, suggesting that its hormone therapy drugs were appropriate
8 for treating or preventing, among other things, memory loss, colon cancer, and age-related
9 vision loss. In the March 19, 2000 edition of *Parade Magazine*, Wyeth spokesperson
10 Lauren Hutton (who was not identified as a Wyeth spokesperson) was asked what she did
11 to look good and feel fit and she answered: "[M]y number 1 secret is estrogen. It's good
12 for your moods, it's good for your skin. If I had to choose between all my creams and
13 makeup for feeling and looking good, I'd take the estrogen."

14 29. A cornerstone of the Defendants' marketing programs was promotion of HRT
15 for long-term use of indefinite duration. Specifically, *JAMA* reported that:

16 In 2000, 46 million prescriptions were written for Premarin
17 (conjugated estrogens), making it the second most frequently
18 prescribed medication in the United States and accounting for
19 more than \$1 billion in sales, and 22.3 million prescriptions were
20 written for Prempro (conjugated estrogens plus
21 medroxyprogesterone acetate). While US Food and Drug
22 Administration-approved indications for hormone therapy
23 include relief of menopausal symptoms and prevention of
24 osteoporosis, *long-term use has been in vogue to prevent a
range of chronic conditions, especially heart disease.*
[Emphasis added.]

25 30. Wyeth continued to press the FDA to approve the use of Prempro to prevent
26 or reduce the progression of heart disease in post-menopausal women. The FDA did not
27 believe there was sufficient scientific evidence to support such an indication/usage of the

1 drug and repeatedly denied Wyeth's request unless Wyeth provided reliable science from a
2 controlled study to support the assertions. Even though the FDA had specifically not
3 approved the use of HRT for the prevention or improvement of heart disease, Wyeth
4 continued to promote Prempro as having this benefit and even represented to physicians
5 that Prempro reduced cardiovascular mortality by 50%.

6 31. In direct to consumer materials, Defendants asserted, inferred or implied that
7 there were heart and mental benefits with HRT. At the same time, Defendants only
8 warned about the risk of uterine cancer (associated with estrogen-only therapy), worsening
9 diabetes, nausea, abdominal pain, irregular bleeding, headache, hair loss, and breast
10 tenderness.

11 32. In the mid 1990s, the Women's Health Initiative Study ("WHI") was started by
12 the National Institutes of Health ("NIH"). This large scale, randomized, controlled study
13 was designed to study the long-term risks and benefits of HRT including heart and mental
14 cognition benefits.

15 33. At the WHI's Data and Safety Monitoring Board ("DSMB") meeting on May
16 31, 2002, it was confirmed that the number of cases of invasive breast cancer in the E+P
17 group had crossed the pre-set safety boundary. The DSMB voted to stop the study based
18 on this finding of increased breast cancer risk in conjunction with the additional evidence of
19 other health risks and an overall lack of long-term benefit. The WHI investigators
20 concluded that, under the circumstances, the risks of taking Prempro outweighed its
21 benefits. The WHI study was stopped early and on July 9, 2002, the NIH released the
22 preliminary results from the study.

23 34. Numerous published scientific papers detail the results of the WHI study,
24 highlight the risks and benefits of E+P and contradict the scientific and medical assertions

1 that Defendants had made for decades about HRT. The Defendants had assured the
2 prescribing physicians that HRT's risks were minimal and that there were great benefits
3 ranging from menopausal symptom relief to the prevention of life threatening medical
4 conditions like heart disease and development of Alzheimer's. Instead the WHI study
5 results showed that there was not a heart benefit from E+P and that E+P may increase the
6 risk of cardiac events in generally healthy post-menopausal women. In addition, the
7 WHIMS arm of the WHI study showed that not only did E+P not improve cognitive function,
8 but E+P users showed a clinically meaningful cognitive decline.

9 35. The WHI study found that for the Prempro arm, when compared to placebo,
10 there was an overall increased risk of the following adverse events:

- 11 a. 41 % increase in strokes;
- 12 b. 29 % increase in heart attacks;
- 13 c. 100 % increase in venous thromboembolism (blood clots);
- 14 d. 22 % increase in total cardiovascular disease; and
- 15 e. 26 % increase in breast cancer.

16
17 The WHI study concluded that the "Overall health risks exceeded benefits from use of
18 combined estrogen plus progestin for an average 5.2-year follow-up among healthy post-
19 menopausal US women." The study also found that the combination hormone regimen
20 should not be initiated or continued for primary prevention of coronary heart disease.

21 36. Because of the importance of the report from the WHI investigators on the
22 estrogen plus progestin study, the study was released early to the public, as an expedited
23 article on the *JAMA* Web site. In commenting on the study's findings, NHLBI Director, Dr.
24 Claude Lenfant, was unequivocal in his own conclusions:

1 The cardiovascular and cancer risks of estrogen plus progestin
2 outweigh any benefits—and a 26 percent increase in breast
3 cancer risk is too high a price to pay, even if there were a heart
benefit. Similarly, the risks outweigh the benefits of fewer hip
fractures.

4 37. Dr. Jacques Roussow, acting director of the WHI and lead author of the
5 JAMA article, summarized the risks of combination hormone therapy in very
6 straightforward manner as he explained the statistical significance of the study results:

7 The WHI results tell us that during 1 year, among 10,000 post-
8 menopausal women with a uterus who are taking estrogen plus
9 progestin, **8 more will have invasive breast cancer, 7 more
10 will have a heart attack, 8 more will have a stroke, and 18
11 more will have blood clots, including 8 with blood clots in
12 the lungs**, than will a similar group of 10,000 women not taking
these hormones. This is a relatively small annual increase in
risk for an individual woman. Individual women who have
participated in the trial and women in the population who have
been on estrogen and progestin should not be unduly alarmed.
However, even small individual risks over time, and on a
population-wide basis, add up to **tens of thousands of these
13 serious adverse health events**. [Emphasis added.]

14 38. It is now clear that HRT poses substantial health risk with little or no
15 corresponding benefit. These risks include breast cancer, ovarian cancer, heart attacks,
16 strokes, deep vein thromboembolisms, pulmonary embolisms, gallbladder cancer and
17 auto-immune diseases (such as lupus and scleroderma).

18 39. **Breast Cancer Risks.** The connection between hormone therapy usage and
19 breast cancer has now been confirmed by dozens of epidemiological studies. In addition,
20 breast cancer caused by E+P is generally detected at a more advanced stage requiring
21 more intensive or invasive treatment. E+P also makes breast tumors harder to detect,
22 leading to dangerous delays in diagnosis. Because E+P increases a woman's breast
23 density and / or stops the natural involution of breast density during menopause, E+P also
24 causes a number of abnormal mammograms requiring unnecessary repeat mammograms.

