Bioidentical Hormones, Estriol, and the FDA

The Women’s Health Initiative study revealed in 2002 that hormone replacement pharmaceuticals, like Premarin (estrogen) and Prempro (estrogen and progestin), increase the risk of stroke and other serious problems. As a result, many women and their doctors turned to compounded bioidentical hormone replacement therapy (BHRT). These custom-made drugs, available only with a licensed practitioner’s prescription, consist of individualized doses of hormones, including estriol, that are chemically identical to human hormones. Estriol is a weak estrogen that gives some protection against breast and endometrial cancers. BHRT is believed to be safer than patented drugs, although no direct comparison studies have been performed. The shift from pharmaceutical products to compounded ones has not gone unnoticed by Wyeth, manufacturer of Premarin, Premphase, and Prempro. Sales of its menopause hormone drugs fell from $2.07 billion in 2001 to $880 million in 2004 (57%).

On October 6, 2005, Wyeth Pharmaceuticals filed a citizen petition with the US Food and Drug Administration (FDA) asking the agency to investigate and take action against compounding pharmacies that promote or dispense compounded bioidentical hormone replacement therapy drugs. The company asserts: “BHRT is a new drug and does not have FDA approval; the BHRT drug is/was compounded ... in a pharmacy that is not required to comply with FDA current good manufacturing practice (CGMP) requirements; and that the BHRT drug has not been demonstrated to be safe or effective for any use, or safer or more effective than FDA-approved hormone therapy drugs.”

Perhaps stunned by an onslaught of over 70,000 comments (most of them against Wyeth’s petition), the FDA did not respond until January 9, 2008. The agency’s response supports compounding pharmacies’ important role as medicine providers for patients who need individualized prescriptions. But the FDA agrees with Wyeth that bioidentical hormone drugs are “new drugs” and “may not be introduced into interstate commerce without FDA approval.” The FDA also agrees with Wyeth that BHRT cannot claim less risk or greater benefit than FDA-approved drugs because the agency is “aware of no adequate randomized, prospective, controlled clinical trials of compounded BHRT drugs that either demonstrate that they are better at relieving menopausal symptoms than a placebo, or that compare them to an FDA-approved drug and establish that the compounded drugs work equally well.” FDA distinguishes between compounding pharmacies that make limited, individualized medicines and those that make bulk products. In a letter to Wyeth’s lawyers, Margaret O’K Glavin, associate commissioner for regulatory affairs, concludes: “Although we share many of your concerns about compounded BHRT drugs, we cannot grant all your requests.” She says that the agency will release a consumer article, press release, and FAQs document as part of a BHRT public awareness campaign.

On the same day as its response to Wyeth’s petition, the FDA sent warning letters to seven compounding pharmacies for making unsupported claims about the safety and effectiveness of BHRT. The FDA considers these claims “false and misleading.” In addition, the agency announced that the use of estriol in any compounded drug is prohibited unless the compounding pharmacy or prescribing doctor has an approved investigation new drug application. “No drug product containing estriol has been approved by FDA,” the agency states, “and the safety and effectiveness of estriol is unknown.” The restriction of estriol hamstrings compounding pharmacies and doctors. Before the FDA ban, an estimated 80% of BHRT drugs contained this weak estrogen. Estriol’s effects and safety have been studied. The International Academy of Compounding Pharmacists’ “Estriol Literature Summation” summarizes 35 clinically relevant studies culled from over 150 articles listed in PubMed and Medline OVID. In addition, estriol has had an official US Pharmacopeia (“USP”) monograph since 1980. Estriol has been approved and marketed as a treatment for postmenopausal symptoms in Europe and Asia for over 40 years. Wyeth itself sells two estriol-containing menopause drugs in Germany.

Several pharmacist associations have protested against the FDA’s ruling. The International Academy of Compounding Pharmacists (IACP) has published several fact sheets and
lobbied Congress to reverse the FDA’s restriction of estriol use. IACP has also met with FDA officials, helped IACP members who received warning letters, and considered possible legal strategies.


Learn Before Choosing Cesarean Section

Because of its physical and emotional consequences, cesarean section has historically been performed only when a mother’s or baby’s safety is threatened; but elective cesarean deliveries (those performed in absence of a medical necessity) have greatly increased in recent years. In 2006, 31.1% of all births in the US were cesarean, a 3% increase from 2005, according to the National Center for Health Statistics. The Pan American Health Organization and US Department of Health and Human Services have set the medically necessary cesarean rate at 15%. A New England Journal of Medicine (NEJM) article (January 8, 2009) based on data from 19 academic medical centers in the US reported that 13,258 of 24,077 women who gave birth through a repeat C-section between 1999 and 2002 chose the procedure; medical necessity did not dictate the surgery. Many factors – including fetal monitoring – have boosted cesarean section rates. Part of the increase may be due to a 2003 policy statement by the American College of Obstetricians and Gynecologists that approves elective cesarean section as a way to support the mother’s autonomy. Also, hospitals and doctors make more money with a cesarean delivery than with a vaginal delivery. The average cost of a cesarean delivery ($12,544 in 2005) is nearly twice the cost of a vaginal delivery ($6,973 in 2005), according to the US Agency for Healthcare Research and Quality.

Women’s requests for an elective cesarean are too often based on incomplete, sometimes inaccurate, knowledge, according to an article in Nursing for Women’s Health (December 2008/January 2009). The article discusses several reasons that healthy women choose to have surgery. Some women (and doctors) believe that cesarean deliveries are “more technologically advanced” and therefore safer. Sometimes fear, stemming from a previous, difficult vaginal delivery, or simply fear of pain associated with vaginal delivery, prompts women to seek an elective cesarean.