



May 8, 2012

Margaret A. Hamburg, M.D.
Commissioner
Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

Re: Safety and effectiveness of bisphosphonates

Dear Commissioner Hamburg,

The National Women's Health Network is a nonprofit advocacy organization that works to improve the health of all women. We bring the voices of women consumers to policy and regulatory decision-making bodies. We are supported by our members and do not take financial contributions from drug companies, medical device manufacturers, insurance companies, or any other entity with a financial stake in women's health decision-making.

We commend the Food and Drug Administration (FDA) for convening the Reproductive Health Drugs and Drug Safety and Risk Management Advisory Committees in September 2011 to assess the safety and effectiveness of long-term use of bisphosphonates. Although the data are not fully mature, serious, and previously unanticipated, risks associated with the drugs have been identified, and there are indications that long-term bisphosphonate use increases those risks. We write today to urge the agency to re-evaluate the balance of risk and benefit for healthy women who are using bisphosphonates to prevent, rather than treat, osteoporosis.

When bisphosphonates were first proposed as a treatment for osteoporosis, we supported the goal of providing women with an alternative to hormone therapy, but we also cautioned that not enough was known about the drugs' long-term effects. Informed by that caution, when the FDA approved the first bisphosphonate in 1995, we advocated for strong post-market surveillance. Since then, several serious side effects have been identified that the clinical trials on which approval was based failed to detect – such as osteonecrosis of the jaw and atypical femur fractures.

In light of this new information, we have serious concerns about the use of bisphosphonates to prevent osteoporosis in healthy women. The inclusion of the prevention indication has affected bisphosphonate use in two important ways: women begin using these drugs at younger ages and, as a

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result may continue using them for several decades, Pharmaceutical companies have engaged in aggressive marketing of the drugs, targeting women in their forties and fifties and also have funded campaigns to promote routine bone density screening of middle-aged women. These campaigns were strikingly effective: an estimated 12% of all women over 55 have received a prescription for bisphosphonates.

While the FDA approved bisphosphonates for the prevention of osteoporosis based on the best science available at the time, the information available today should lead to a different conclusion. The evidence to support the use of bisphosphonates for the treatment of osteoporosis in post-menopausal women is still strong. Emerging evidence, however, suggests that use beyond the recommended three to five years results in increased risk of atypical femur fractures, as well as other serious adverse events. While the exact length of appropriate use may not yet be certain, the need for caution about long-term use is clear. Therefore, the question of when women begin using bisphosphonates is critical, and the prevention indication is problematic because it affects prescribing in ways that encourage long-term use.

We urge the FDA to remove the prevention indication for bisphosphonates and to take steps to alert women and their health care providers that these drugs are no longer recommended for prevention of osteoporosis. Agency actions should include changing the label, as well as sending out 'Dear Doctor' letters to ensure that health care providers have the most up to date information when discussing osteoporosis treatment options with their female patients.

The addition of information about the risks associated with the drug to the label was an essential step toward ensuring women's informed decision-making, but further action is needed to reduce unnecessary exposure to these risks. Healthy women have better, less risky, ways to protect themselves from bone fractures and should not be encouraged to take drugs which could so seriously undermine their goal of maintaining healthy bones.

Sincerely,



Cynthia A. Pearson
Executive Director
National Women's Health Network

Cc: Janet Woodcock, M.D., Director, Center for Drug Evaluation and Research, Food and Drug Administration

Cc: Marsha Henderson, MCRP, Assistant Commissioner for Women's Health, Office of Women's Health, Food and Drug Administration