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Stronger Cautions Backed on Bone Drugs for Women

By DUFF WILSON

Two advisory panels to the Food and Drug Administration on Friday recommended increasing the cautionary language on the product labels of bone-building drugs taken by more than five million women in the United States.

But they stopped short of specifying what the safety warnings should say and did not recommend limiting use of the drugs to a proposed five years. About 11 percent of women 55 and older take the drugs to prevent bone fractures.

The medical advisers did not press the issue as strongly as the F.D.A. staff itself did in a 45-page report issued on Wednesday. The staff report said studies "suggest no significant advantage of continuing drug therapy beyond five years."

The F.D.A. is expected to issue a revised label in November

for the drugs, known as bisphosphonates, including Fosamax, Actonel and Boniva.

The agency usually follows the advice of its advisory panels, but not always.

The two panels met jointly on Friday to comment on the staff's broad safety review of the drugs, prompted by concerns over a relatively small number of long-term users who had suffered unusual thigh fractures or a serious jaw disease. The benefits of the drugs have only been proven for three to five years, not longer, F.D.A. staff members said, warning about links to those rare conditions after longer use.

The advisory meeting ended in a 17-6 vote on a single question put to the panel for a vote: whether the labels should "further clarify the duration of use" of the drugs. Several advisers said the question was vague. So are the current labels, which say, "The optimal duration of use has not been determined."

The F.D.A. said an estimated 9 percent of users take the drugs longer than three years, and under 1 percent take them longer than five years.

But none of the panel members recommended firm restrictions on longer-term use. None suggested a so-called black box warning, as some former patients who suffered the

injuries are seeking.

Dr. Lewis S. Nelson, a toxicologist with the New York University School of Medicine, said the evidence warranted "something a little bit more dramatic," like moving the statement to the "warnings" section of the label from the section on "indications and usage."

Others said few patients heeded the label, anyway. They suggested stronger language asking doctors to review the usage annually.

Dr. Nelson is chairman of the F.D.A. Drug Safety and Risk Management Committee; it joined the Advisory Committee for Reproductive Health Drugs in the daylong review.

Dr. Clifford J. Rosen, a professor at the Tufts University School of Medicine, who voted for the new label, opposed a tougher warning for people to stop taking the drugs.

"I wouldn't put a limit of five years for therapy because that would handcuff a lot of doctors," he said.

Several advisers said the new label needed to be much more specific about benefits during the first three to five years and about the uncertainties after that. They said doctors and patients should consider a variety of factors while individually considering longer-term use of the drug.

The six people who voted against a label change said there was insufficient evidence of risk in longer use, especially with a drug proven to benefit women for the first three to five years.

“I don’t want to cry wolf on this,” said Dr. John M. Kittelson, a professor in the Department of Biostatistics and Informatics at the University of Colorado Denver.

Several women who have suffered the unusual fractures testified at the meeting.

Dr. Jennifer P. Schneider, whose thigh broke as she was standing in a New York subway, presented her own review of 111 cases.

Almost all took the drug for more than five years, most for a pre-osteoporosis condition called osteopenia, she said. Many felt pain in the thigh before the bone suddenly broke.

The first such drug, Fosamax, was marketed by Merck in 1995. Others include Actonel and Atelvia from Warner Chilcott and Boniva from Roche Therapeutics. Worldwide sales last year were $7.6 billion.

The committee also called for more study of the overall effectiveness of the drugs in their desired goal of preventing fractures. And the advisers recommended that the F.D.A. take a close look at why the drugs are prescribed as

preventive medicine for women who do not even have osteoporosis.