

Alendronate Favored to Prevent Fragility Fractures

BY JONATHAN GARDNER
London Bureau

Physicians should favor prescribing alendronate for secondary prevention of osteoporotic fragility fractures unless patients cannot take the medication, the clinical effectiveness agency for England and Wales has ruled.

The National Institute for Health and Clinical Excellence's final assessment of preventive drugs for postmenopausal women "who have osteoporosis and have sustained a clinically apparent osteoporotic fragility fracture" also allows other bisphosphonates—along with strontium

ranelate, raloxifene, and teriparatide—if patients are intolerant to alendronate, have a contraindication, or cannot comply with the instructions for taking alendronate.

In the event that patients cannot take alendronate, NICE's guideline recommends risedronate and etidronate. A patient's intolerance to etidronate and risedronate allows physicians to move on to strontium ranelate and raloxifene, provided the patient has additional risk factors or meets a stricter bone mineral density threshold.

Teriparatide is recommended if patients have a contraindication, intolerance, or unsatisfactory response to the other drugs and have a combination of very low T

scores and at least two fragility fractures.

Alendronate, the least expensive medication (at £53.56 for once-weekly tablets for the generic version), was the most cost effective and was no less effective than were alternatives in preventing fragility fractures in the population, according to the NICE panel that assessed the medications.

But the panel was able to develop thresholds for the use of alternative medications, based on age, clinical risk factors, and T scores, that would not increase the National Health Service's costs by more than £30,000 per quality-adjusted life-year gained.

For example, women aged 55-59 years must have a T score of -3 to qualify for the

use of risedronate or etidronate if they do not have an independent risk factor, whereas women aged 70 years or older must have a T score of only -2.5. Women aged 50-54 years do not qualify for any of the alternative medications unless they have an independent clinical risk factor.

The guideline assumes patients are receiving adequate calcium and vitamin D. It also states that a dual-energy x-ray absorptiometry scan may not be necessary for patients 75 years and older, or patients with body mass index lower than 22 kg/m² and ankylosing spondylitis, Crohn's disease, disorders requiring prolonged immobility, and untreated premature menopause. ■

FRAX Fracture Risk Assessment Tool Shines in Two Case Studies

BY DOUG BRUNK
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CALGARY, ALTA. — Two case studies illustrate the benefits of the osteoporosis risk assessment tool known as FRAX.

The brain child of the World Health Organization's Dr. John A. Kanis, FRAX is a computerized assessment tool that combines bone mineral density at the femoral neck with clinical risk factors to help clinicians determine a patient's 10-year risk of osteoporotic fractures.

The National Osteoporosis Foundation's Clinician's Guide to Prevention and Treatment of Osteoporosis (www.nof.org/professionals/Clinicians_Guide.htm) has recommendations on bone mineral density testing and other evaluation methods for the prevention of osteoporosis.

For example, the guidelines recommend that postmenopausal women, and men aged 50 and older, should be treated when they present with:

- ▶ A hip or vertebral (clinical or morphometric) fracture.
- ▶ Other prior fractures and low bone mass (T score between -1.0 and -2.5 at the femoral neck, total hip, or spine).
- ▶ T score of -2.5 or less at the femoral neck, total hip, or spine after appropriate evaluation to exclude secondary causes.
- ▶ Low bone mass (T score between -1.0 and -2.5 at the femoral neck, total hip, or spine) and secondary causes associated with high risk of fracture (such as glucocorticoid use or total immobilization).
- ▶ A 10-year probability of hip fracture of 3% or greater or a 10-year probability of any major osteoporosis-related fracture of 20% or greater based on the FRAX tool.

Dr. David L. Kendler, who also directs the Osteoporosis Center of British Columbia and is a past president of the International Society for Clinical Densitometry, offered two case examples based on these recommendations. The first is a 54-year-old female smoker with a T score of -2.0. "Her 10-year overall fracture risk would be about 10% and her 10-year hip fracture risk would be about 2.5%, so you would not treat this patient," he said.

The other example is 81-year-old female with a T score of -1.4. "Her 10-year overall fracture risk is 25% and her 10-year hip fracture risk would be

about 3.2%, so you would treat this patient," said Dr. Kendler, speaking at the annual clinical meeting of the Society of Obstetricians and Gynaecologists of Canada.

FRAX was developed using population-based cohort studies from Europe, North America, Asia, and Australia that represent 249,898 person-years of data. The user is asked to complete fields for age, gender, weight, height, and femoral neck bone mineral density, and to answer yes or no to the following risk factors: previous fracture, parental history of fracture, current tobacco smoker, history of long-term use of glucocorticoids, rheumatoid arthritis, and alcohol intake of three or more units per day.

The user then presses the "calculate" button and the software program provides a 10-year probability of hip fracture and a 10-year probability of a major osteoporotic fracture, defined as one that involves the clinical spine, forearm, hip, or shoulder.

Dr. Kendler, an endocrinologist who is associate professor of medicine at the University of British Columbia, Vancouver, said that the combination of bone mineral density and clinical risk factors "allows us to identify patients at higher risk of osteoporotic fracture. We have moved toward using an intervention threshold based on fracture probability. Treatment will be targeted to patients who will receive the greatest therapeutic benefit."

According to the International Society for Clinical Densitometry, indications for bone mineral density testing include women age 65 and older; postmenopausal women under age 65 with risk factors; men aged 70 and older; adults with a frailty fracture; adults with a disease or condition associated with low bone mass or bone loss; adults taking medications associated with low bone mass or bone loss; anyone being considered for pharmacologic therapy; anyone being treated for low bone mass, to monitor treatment effect; and anyone not receiving therapy in whom evidence of bone loss would lead to treatment.

Dr. Kendler disclosed receiving grants and/or honoraria from Merck & Co., Eli Lilly & Co., Novartis, Wyeth, Pfizer Inc., Takeda Pharmaceutical Co., and GlaxoSmithKline. The presentation was sponsored by Eli Lilly Canada Inc. ■



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DR. KENDLER

Yearly Zoledronic Acid Cut Back-Related Disability

BY HEIDI SPLETE
Senior Writer

WASHINGTON — A yearly dose of zoledronic acid significantly reduced the number of days of disability because of back pain in older women with osteoporotic fractures, based on data from the HORIZON Pivotal Fracture study.

"Osteoporotic fractures can result in back pain, significant disability, reduced quality of life, and death," Jane A. Cauley, Dr.PH, of the University of Pittsburgh, wrote in a poster at the annual meeting of the American Geriatrics Society.

In the HORIZON Pivotal Fracture Study, a randomized, controlled trial of more than 7,000 postmenopausal women aged 65-79 years, a yearly dose of 5 mg zoledronic acid significantly reduced all types of clinical fractures, compared with placebo. The drug was administered in a 15-minute intravenous infusion.

In the current study, funded by Novartis Pharma AG in Basel, Switzerland, the researchers compared the effect of the yearly dose of zoledronic acid on the number of days of disability, bed rest, and back pain. The intent-to-treat population included 3,875 women who received zoledronic acid and 3,861 who received a placebo. The researchers collected information on days of limited activity and bed rest due to an osteoporotic fracture or back pain every 3 months over a 3-year period.

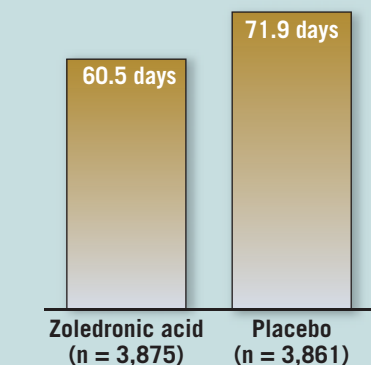
Older age and a prevalent vertebral fracture were significantly associated with more days of bed rest, back pain, and fracture-related disability.

Overall, women who took zoledronic acid averaged significantly fewer bed rest days because of fracture, versus the placebo group (1.6 days vs. 2.2 days, respectively) and significantly fewer limited-activity days because of fracture, compared with the placebo group (5.9

days vs. 9.9 days). Similarly, women who took zoledronic acid averaged significantly fewer bed rest days because of back pain, compared with those in the placebo group (8.2 days vs. 9.2 days, respectively) and significantly fewer limited-activity days because of back pain, compared with the placebo group (60.5 days vs. 71.9 days).

After controlling for incident clinical fracture, the drug remained significantly tied to fewer days of limited activity. ■

Limited-Activity Days Because Of Back Pain in Women With Osteoporotic Fractures



Note: Based on a 3-year study of women aged 65-79 years.
Source: Dr. Cauley