

New Study Comparing Weekly Osteoporosis Treatments Shows FOSAMAX® Demonstrated Significantly Greater Increases in Bone Mineral Density and Reductions in Markers of Bone Turnover than Actonel®

FOSAMAX® (alendronate sodium) Maintained or Increased BMD at Hip and Spine for Significantly More Patients than Actonel® (risedronate), with Similar Tolerability, in this 12 Month Study

MONTREAL, CANADA, October 13, 2004 - FOSAMAX® Once Weekly (alendronate sodium) increased bone mineral density (BMD) more than Actonel® Once-a-Week (risedronate) with similar tolerability, according to results of the FOSAMAX Actonel Comparison Trial (FACT). This is the first U.S. head-to-head study comparing once weekly osteoporosis treatments in postmenopausal women with osteoporosis. In this study, alendronate sodium provided greater increases in BMD at all sites measured as early as six months, and lowered levels of biochemical markers of bone turnover further within the normal pre-menopausal range than risedronate within three months. Reducing and stabilizing bone turnover, which leads to increased bone density, are important factors in improving bone strength in patients with osteoporosis.

The results of FACT, which was a 12 month study, were announced [earlier this week] online in the Journal of Bone and Mineral Research. A 12-month extension of this double-blind study, and a second similarly designed study, are currently underway.

“In this 12-month study, alendronate sodium demonstrated greater increases in BMD and reductions in bone turnover and similar tolerability compared to risedronate,” said Marc Hochberg, MD, professor of medicine and epidemiology and Preventive Medicine at the University of Maryland-School of Medicine in Baltimore. “Studies like FACT, that make direct “head-to-head” comparisons between treatments, are important because they provide important information to clinicians for use in making treatment decisions for postmenopausal women with osteoporosis.”

In the FACT trial, alendronate sodium increased BMD more than risedronate

Alendronate sodium showed greater increases in BMD at all pre-specified study endpoints compared to risedronate. Study results showed that alendronate sodium increased BMD 62 percent more than risedronate at the hip trochanter, a specific region of the hip, at 12 months (3.4 percent increase for alendronate sodium vs. 2.1 percent for risedronate; $p < 0.001$), the primary endpoint of the study. For other sites, alendronate

sodium increased BMD 83 percent more than risedronate at the total hip (2.2 percent vs. 1.2 percent; $p < 0.001$), 78 percent more at the femoral neck (1.6 percent vs. 0.9 percent; $p = 0.005$), and 42 percent more at the lumbar spine (3.7 percent vs. 2.6 percent; $p < 0.001$). These differences in BMD between alendronate sodium and risedronate were statistically significant as early as six months.

In addition, more patients taking alendronate sodium maintained or increased BMD after 12 months than did patients taking risedronate. Specifically, 84.5 percent of ($n = 392$) patients on alendronate sodium gained or maintained BMD at the hip trochanter versus 67.8 percent of ($n = 326$) risedronate patients ($p < 0.001$), and 87.3 percent of patients ($n = 407$) taking alendronate sodium maintained or gained BMD at the lumbar spine versus 75.6 percent of risedronate patients ($n = 365$) ($p < 0.001$).

The overall incidence of clinical adverse experiences (AEs) were similar between the two groups, with upper gastrointestinal AEs occurring in 22.5 percent and 20.1 percent of the patients in the alendronate sodium and risedronate groups, respectively ($p = 0.364$). Drug related AE's greater than or equal to one percent in either treatment group in this study, included abdominal pain, diarrhea, constipation, heartburn/dyspepsia, flatulence, nausea, vomiting, joint pain, muscle pain, and headache.

Study shows significant differences between treatments in biochemical markers, as early as three months

It has been established that women with osteoporosis have accelerated bone turnover, with the result that the amount of new bone produced is insufficient to replace the amount of bone that is "resorbed," or broken down. In this study, as early as three months, alendronate sodium demonstrated significantly greater changes in bone markers indicative of decreased turnover compared to risedronate. One marker, serum CTx, a test that measures bone resorption, decreased by 73.8 percent for patients taking alendronate sodium versus 54.7 percent for patients taking risedronate ($p < 0.001$).

This one-year randomized, double-blind, multi-center, head-to-head trial of 1,053 postmenopausal osteoporotic women with low BMD (T-score less than or equal to -2.0 at either hip trochanter, total hip, femoral neck or spine) compared the effects of alendronate sodium 70 mg Once-Weekly to risedronate 35 mg Once-A-Week on BMD,

bone turnover and tolerability. The primary endpoint was change from baseline in BMD at the hip trochanter at 12 months. Secondary endpoints included BMD at the hip, femoral neck and spine, markers of bone turnover, and tolerability as assessed by AE reporting. BMD was measured at baseline and again at six and 12 months of treatment, while changes in bone turnover were measured at baseline and again at three, six and 12 months. Study participants had a mean age of 65 years and were instructed to take 1,000 mg of calcium daily and 400 I.U. of vitamin D either from food or a supplement.

About Osteoporosis, Bone Mineral Density and Bone Turnover

Osteoporosis is a chronic condition that can lead to bone loss and susceptibility to fractures. Over 10 million people in the U.S. are estimated to have osteoporosis and another 34 million are estimated to have low bone mass. The majority are women. These women can experience one-third of their lifetime bone loss within the first five years after menopause. The loss of bone mass that can occur after menopause increases the risk that a woman will develop osteoporosis and related fractures. One in two women over age 50 will have an osteoporosis-related fracture in her lifetime.

BMD measures the density of bone and is the standard measurement to diagnose osteoporosis. BMD is a major determinant of bone strength. The lower the BMD score the greater the risk of fracture.

Whereas BMD measures bone strength, bone turnover markers measure the rate at which bone is broken down and formed. An increase in bone turnover is common after menopause. Antiresorptive agents such as alendronate sodium increase BMD and decrease bone turnover, and thus help to restore the balance between bone loss and bone formation.

Important information about alendronate sodium

Alendronate sodium, like other bisphosphonates, should be used with caution in people with certain stomach or digestive problems. Alendronate sodium should not be used if the patient has certain disorders of the esophagus that delay emptying or if the patient is unable to stand or sit upright for at least 30 minutes. In addition, alendronate sodium should not be used in patients with severe kidney disease or low levels of calcium in their blood, in patients who are allergic to alendronate sodium or in patients who are

pregnant or nursing. Patients who have difficulty swallowing liquids should not take alendronate sodium oral solution.

Some patients may develop severe digestive reactions including irritation, inflammation or ulceration of the esophagus. The risk of severe esophageal experiences appears to be greater in patients who fail to follow dosing instructions (see prescribing information for more details). Patients who experience new or worsening heartburn, difficulty or pain when swallowing or chest pain should stop taking the drug and consult their doctor. The most commonly reported side effects with alendronate sodium in other clinical studies have been abdominal pain, musculoskeletal pain, indigestion, regurgitation and nausea.

FOSAMAX is a medicine from Merck Frosst

Introduced in Canada in 1996 for the treatment of postmenopausal osteoporosis, alendronate sodium is approved for: the treatment of Paget's disease of bone (40 mg once daily); the prevention of osteoporosis in postmenopausal women at risk of osteoporosis (5 mg once daily, 35 mg once weekly); the treatment of postmenopausal osteoporosis and the reduction in the incidence of hip and spine fractures in postmenopausal women who have osteoporosis (10 mg once daily, 70 mg once weekly).

In addition, alendronate sodium is approved for the treatment of glucocorticoid-induced osteoporosis in men and women receiving glucocorticoids in a daily dosage equivalent to 7.5 mg or greater of prednisone and who have low bone mineral density (5 mg once daily, except for postmenopausal women not receiving estrogen, for whom the recommended dosage is 10 mg once daily); and for the treatment to increase bone mass in men with osteoporosis (10 mg once daily, 70 mg once weekly).

About Merck Frosst

Merck Frosst is one of the country's leading research-based pharmaceutical companies. In 2003, the company invested \$116 million in research and development in Canada. Merck Frosst Canada & Co. and Merck Frosst Canada Ltd. are affiliated companies of Merck & Co., Inc. of Whitehouse Station, New Jersey, which is a publicly traded company on the New York Stock Exchange under the symbol MRK. More information about Merck Frosst is available at <http://www.merckfrosst.com>

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