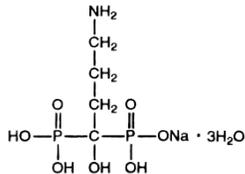




MERCK & CO., INC.
Whitehouse Station, NJ 08889, USA

FOSAMAX®
(ALENDRONATE SODIUM)
TABLETS AND ORAL SOLUTION

DESCRIPTION
FOSAMAX® (alendronate sodium) is a bisphosphonate that acts as a specific inhibitor of osteoclast-mediated bone resorption. Bisphosphonates are synthetic analogs of pyrophosphate that bind to the hydroxyapatite found in bone. Alendronate sodium is chemically described as (4-amino-1-hydroxybutylidene) bisphosphonic acid monosodium salt trihydrate. The empirical formula of alendronate sodium is C₁₄H₁₂NNaO₇P₂·3H₂O and its formula weight is 325.12. The structural formula is:



Alendronate sodium is a white, crystalline, nonhygroscopic powder. It is soluble in water, very slightly soluble in alcohol, and practically insoluble in chloroform. Tablets FOSAMAX for oral administration contain 6.53, 13.05, 45.58, 52.21 or 91.37 mg of alendronate monosodium salt trihydrate, which is the molar equivalent of 5, 10, 35, 40 and 70 mg, respectively, of free acid, and the following inactive ingredients: microcrystalline cellulose, anhydrous lactose, croscarmellose sodium, and magnesium stearate. Tablets FOSAMAX 10 mg also contain carnauba wax. Each bottle of the oral solution contains 91.35 mg of alendronate monosodium salt trihydrate, which is the molar equivalent to 70 mg of free acid. Each bottle also contains the following inactive ingredients: sodium citrate dihydrate and citric acid anhydrous as buffering agents, sodium saccharin, artificial raspberry flavor, and purified water. Added as preservatives are sodium propylparaben 0.0225% and sodium butylparaben 0.0075%.

CLINICAL PHARMACOLOGY

Mechanism of Action
Animal studies have indicated the following mode of action. At the cellular level, alendronate shows preferential localization to sites of bone resorption, specifically under osteoclasts. The osteoclasts adhere normally to the bone surface but lack the ruffled border that is indicative of active resorption. Alendronate does not interfere with osteoclast recruitment or attachment, but it does inhibit osteoclast activity. Studies in mice on the localization of radioactive [³H]alendronate in bone showed about 10-fold higher uptake on osteoclast surfaces than on osteoblast surfaces. Bones examined 6 and 49 days after [³H]alendronate administration in rats and mice, respectively, showed that normal bone was formed on top of the alendronate, which was incorporated inside the matrix. While incorporated in bone matrix, alendronate is not pharmacologically active. Thus, alendronate must be continuously administered to suppress osteoclasts on newly formed resorption surfaces. Histomorphometry in baboons and rats showed that alendronate treatment reduces bone turnover (i.e., the number of sites at which bone is remodeled). In addition, bone formation exceeds bone resorption at these remodeling sites, leading to progressive gains in bone mass.

Pharmacokinetics
Absorption
Relative to an intravenous (IV) reference dose, the mean oral bioavailability of alendronate in women was 0.64% for doses ranging from 5 to 70 mg when administered after an overnight fast and two hours before a standardized breakfast. Oral bioavailability of the 10 mg tablet in men (0.59%) was similar to that in women when administered after an overnight fast and 2 hours before breakfast. FOSAMAX 70 mg oral solution and FOSAMAX 70 mg tablet are equally bioavailable.

A study examining the effect of timing of a meal on the bioavailability of alendronate was performed in 49 postmenopausal women. Bioavailability was decreased (by approximately 40%) when 10 mg alendronate was administered either 0.5 or 1 hour before a standardized breakfast, when compared to dosing 2 hours before eating. In studies of treatment and prevention of osteoporosis, alendronate was effective when administered at least 30 minutes before breakfast. Bioavailability was negligible whether alendronate was administered with or up to two hours after a standardized breakfast. Concomitant administration of alendronate with coffee or orange juice reduced bioavailability by approximately 60%.

Distribution
Preclinical studies (in male rats) show that alendronate transiently distributes to soft tissues following 1 mg/kg IV administration but is then rapidly redistributed to bone or excreted in the urine. The mean steady-state volume of distribution, exclusive of bone, is at least 28 L in humans. Concentrations of drug in plasma following therapeutic oral doses are too low (less than 5 ng/mL) for analytical detection. Protein binding in human plasma is approximately 78%.

Metabolism
There is no evidence that alendronate is metabolized in animals or humans.

Excretion
Following a single IV dose of [¹⁴C]alendronate, approximately 50% of the radioactivity was excreted in the urine within 72 hours and little or no radioactivity was recovered in the feces. Following a single 10 mg IV dose, the renal clearance of alendronate was 71 mL/min (64, 76, 90% confidence interval [CI]), and systemic clearance did not exceed 200 mL/min. Plasma concentrations fell by more than 95% within 6 hours following IV administration. The terminal half-life in humans is estimated to exceed 10 years, probably reflecting release of alendronate from the skeleton. Based on the above, it is estimated that after 10 years of oral treatment with FOSAMAX (10 mg daily) the amount of alendronate released daily from the skeleton is approximately 25% of that absorbed from the gastrointestinal tract.

Special Populations
Pediatric: Alendronate pharmacokinetics have not been investigated in patients <18 years of age.
Gender: Bioavailability and the fraction of an IV dose excreted in urine were similar in men and women.
Geriatric: Bioavailability and disposition (urinary excretion) were similar in elderly and younger patients. No dosage adjustment is necessary (see DOSAGE AND ADMINISTRATION).

Race: Pharmacokinetic differences due to race have not been studied.
Renal Insufficiency: Preclinical studies show that, in rats with kidney failure, increasing amounts of drug are present in plasma, kidney, spleen, and tibia. In healthy controls, drug that is not deposited in bone is rapidly excreted in the urine. No evidence of saturation of bone uptake was found after 3 weeks dosing with cumulative IV doses of 35 mg/kg in young male rats. Although no clinical information is available, it is likely that, as in animals, elimination of alendronate via the kidney will be reduced in patients with impaired renal function. Therefore, somewhat greater

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accumulation of alendronate in bone might be expected in patients with impaired renal function. No dosage adjustment is necessary for patients with mild-to-moderate renal insufficiency (creatinine clearance 35 to 60 mL/min). **FOSAMAX is not recommended for patients with more severe renal insufficiency (creatinine clearance <35 mL/min) due to lack of experience with alendronate in renal failure.**
Hepatic Insufficiency: As there is evidence that alendronate is not metabolized or excreted in the bile, no studies were conducted in patients with hepatic insufficiency. No dosage adjustment is necessary.

Drug Interactions (also see PRECAUTIONS, Drug Interactions)
Intravenous ranitidine was shown to double the bioavailability of oral alendronate. The clinical significance of this increased bioavailability and whether similar increases will occur in patients given oral H₂-antagonists is unknown.
In healthy subjects, oral prednisone (20 mg three times daily for five days) did not produce a clinically meaningful change in the oral bioavailability of alendronate (a mean increase ranging from 20 to 44%).
Products containing calcium and other multivalent cations are likely to interfere with absorption of alendronate.

Pharmacodynamics
Alendronate is a bisphosphonate that binds to bone hydroxyapatite and specifically inhibits the activity of osteoclasts, the bone-resorbing cells. Alendronate reduces bone resorption with no direct effect on bone formation, although the latter process is ultimately reduced because bone resorption and formation are coupled during bone turnover.

Osteoporosis in postmenopausal women
Osteoporosis is characterized by low bone mass that leads to an increased risk of fracture. The diagnosis can be confirmed by the finding of low bone mass, evidence of fracture on x-ray, a history of osteoporotic fracture, or height loss or kyphosis, indicative of vertebral (spinal) fracture. Osteoporosis occurs in both males and females but is most common among women following the menopause, when bone turnover increases and the rate of bone resorption exceeds that of bone formation. These changes result in progressive bone loss and lead to osteoporosis in a significant proportion of women over age 50. Fractures, usually of the spine, hip, and wrist, are the common consequences. From age 50 to age 90, the risk of hip fracture in white women increases 50-fold and the risk of vertebral fracture 15- to 30-fold. It is estimated that approximately 40% of 50-year-old women will sustain one or more osteoporosis-related fractures of the spine, hip, or wrist during their remaining lifetimes. Hip fractures, in particular, are associated with substantial morbidity, disability, and mortality.

Daily oral doses of alendronate (5, 20, and 40 mg for six weeks) in postmenopausal women produced biochemical changes indicative of dose-dependent inhibition of bone resorption, including decreases in urinary calcium and urinary markers of bone collagen degradation (such as deoxypyridinoline and cross-linked N-telopeptides of type I collagen). These biochemical changes tended to return toward baseline values as early as 3 weeks following the discontinuation of therapy with alendronate and did not differ from placebo after 7 months.

Long-term treatment of osteoporosis with FOSAMAX 10 mg/day (for up to five years) reduced urinary excretion of markers of bone resorption, deoxypyridinoline and cross-linked N-telopeptides of type I collagen, by approximately 50% and 70%, respectively, to reach levels similar to those seen in healthy premenopausal women. Similar decreases were seen in patients in osteoporosis prevention studies who received FOSAMAX 5 mg/day. The decrease in the rate of bone resorption indicated by these markers was evident as early as one month and at three to six months reached a plateau that was maintained for the entire duration of treatment with FOSAMAX. In osteoporosis treatment studies FOSAMAX 10 mg/day decreased the markers of bone formation, osteocalcin and bone specific alkaline phosphatase by approximately 50%, and total serum alkaline phosphatase by approximately 25 to 30% to reach a plateau after 6 to 12 months. In osteoporosis prevention studies FOSAMAX 5 mg/day decreased osteocalcin and total serum alkaline phosphatase by approximately 40% and 15%, respectively. Similar reductions in the rate of bone turnover were observed in postmenopausal women during one-year studies with once weekly FOSAMAX 70 mg for the treatment of osteoporosis and once weekly FOSAMAX 35 mg for the prevention of osteoporosis. These data indicate that the rate of bone turnover reached a new steady-state, despite the progressive increase in the total amount of alendronate deposited within bone.

As a result of inhibition of bone resorption, asymptomatic reductions in serum calcium and phosphate concentrations were also observed following treatment with FOSAMAX. In the long-term studies, reductions from baseline in serum calcium (approximately 2%) and phosphate (approximately 4 to 8%) were evident the first month after the initiation of FOSAMAX 10 mg. No further decreases in serum calcium were observed during the five-year duration of treatment, however, serum phosphate returned toward prestudy levels during years three through five. Similar reductions were observed with FOSAMAX 5 mg/day. In one-year studies with once weekly FOSAMAX 35 and 70 mg, similar reductions were observed at 6 and 12 months. The reduction in serum phosphate may reflect not only the positive bone mineral balance due to FOSAMAX but also a decrease in renal phosphate reabsorption.

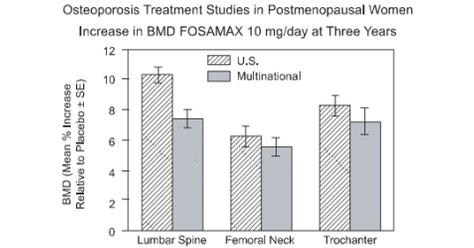
Osteoporosis in men
Treatment of men with osteoporosis with FOSAMAX 10 mg/day for two years reduced urinary excretion of cross-linked N-telopeptides of type I collagen by approximately 60% and bone-specific alkaline phosphatase by approximately 40%. Similar reductions were observed in a one-year study in men with osteoporosis receiving once weekly FOSAMAX 70 mg.

Glucocorticoid-induced Osteoporosis
Sustained use of glucocorticoids is commonly associated with development of osteoporosis and resulting fractures (especially vertebral, hip, and rib). It occurs both in males and females of all ages. Osteoporosis occurs as a result of inhibited bone formation and increased bone resorption resulting in net bone loss. Alendronate decreases bone resorption without directly inhibiting bone formation.
In clinical studies of up to two years' duration, FOSAMAX 5 and 10 mg/day reduced cross-linked N-telopeptides of type I collagen (a marker of bone resorption) by approximately 60% and reduced bone-specific alkaline phosphatase and total serum alkaline phosphatase (markers of bone formation) by approximately 15 to 30% and 8 to 18%, respectively. As a result of inhibition of bone resorption, FOSAMAX 5 and 10 mg/day induced asymptomatic decreases in serum calcium (approximately 1 to 2%) and serum phosphate (approximately 1 to 8%).

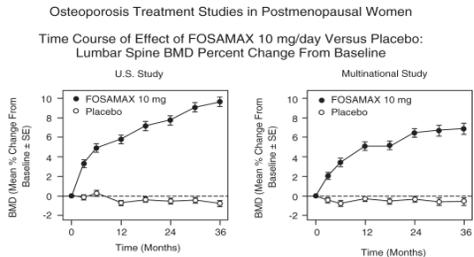
Paget's disease of bone
Paget's disease of bone is a chronic, focal skeletal disorder characterized by greatly increased and disorderly bone remodeling. Excessive osteoclastic bone resorption is followed by osteoblastic new bone formation, leading to the replacement of the normal bone architecture by disorganized, enlarged, and weakened bone structure. Clinical manifestations of Paget's disease range from no symptoms to severe morbidity due to bone deformity, pathological fractures, and neurological and other complications. Serum alkaline phosphatase, the most frequently used biochemical index of disease activity, provides an objective measure of disease severity and response to therapy.
FOSAMAX decreases the rate of bone resorption directly, which leads to an indirect decrease in bone formation. In clinical trials, FOSAMAX 40 mg once daily for six months produced significant decreases in serum alkaline phosphatase as well as in urinary markers of bone collagen degradation. As a result of the inhibition of bone resorption, FOSAMAX induced generally mild, transient, and asymptomatic decreases in serum calcium and phosphate.

Clinical Studies
Treatment of osteoporosis
Postmenopausal women
Effect on bone mineral density
The efficacy of FOSAMAX 10 mg once daily in postmenopausal women, 44 to 84 years of age, with osteoporosis (lumbar spine bone mineral density [BMD] of at least 2 standard deviations below the premenopausal mean) was demonstrated in four double-blind, placebo-controlled clinical studies of two or three years' duration. These included two three-year, multicenter studies of virtually identical design, one performed in the United States (U.S.) and the other in 15 different countries (Multinational), which enrolled 478 and 516 patients, respectively. The following graph shows the mean increases in BMD of the lumbar spine, femoral neck, and trochanter in patients receiving FOSAMAX 10 mg/day relative to placebo-treated patients at three years for each of these studies.

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At three years significant increases in BMD, relative both to baseline and placebo, were seen at each measurement site in each study in patients who received FOSAMAX 10 mg/day. Total body BMD also increased significantly in each study, suggesting that the increases in bone mass of the spine and hip did not occur at the expense of other skeletal sites. Increases in BMD were evident as early as three months and continued throughout the three years of treatment. (See figures below for lumbar spine results.) In the two-year extension of these studies, treatment of 147 patients with FOSAMAX 10 mg/day resulted in continued increases in BMD at the lumbar spine and trochanter (absolute additional increases between years 3 and 5: lumbar spine, 0.94%; trochanter, 0.88%). BMD at the femoral neck, forearm and total body were maintained. FOSAMAX was similarly effective regardless of age, race, baseline rate of bone turnover, and baseline BMD in the range studied (at least 2 standard deviations below the premenopausal mean). Thus, overall FOSAMAX reverses the loss of bone mineral density, a central factor in the progression of osteoporosis.



In patients with postmenopausal osteoporosis treated with FOSAMAX 10 mg/day for one or two years, the effects of treatment withdrawal were assessed. Following discontinuation, there were no further increases in bone mass and the rates of bone loss were similar to those of the placebo groups. These data indicate that continued treatment with FOSAMAX is required to maintain the effect of the drug.
The therapeutic equivalence of once weekly FOSAMAX 70 mg (n=519) and FOSAMAX 10 mg daily (n=370) was demonstrated in a one-year, double-blind, multicenter study of postmenopausal women with osteoporosis. In the primary analysis of completers, the mean increases from baseline in lumbar spine BMD at one year were 5.1% (4.8, 5.4%; 95% CI) in the 70-mg once-weekly group (n=440) and 5.4% (5.0, 5.8%; 95% CI) in the 10-mg daily group (n=330). The two treatment groups were also similar with regard to BMD increases at other skeletal sites. The results of the intention-to-treat analysis were consistent with the primary analysis of completers.

Effect on fracture incidence
Data on the effects of FOSAMAX on fracture incidence are derived from three clinical studies: 1) U.S. and Multinational combined; a study of patients with a BMD T-score at or below minus 2.5 with or without a prior vertebral fracture, 2) Three-Year Study of the Fracture Intervention Trial (FIT); a study of patients with at least one baseline vertebral fracture, and 3) Four-Year Study of FIT; a study of patients with low bone mass but without a baseline vertebral fracture.
To assess the effects of FOSAMAX on the incidence of vertebral fractures (detected by digitized radiography; approximately one third of these were clinically symptomatic), the U.S. and Multinational studies were combined in an analysis that compared placebo to the pooled dosage groups of FOSAMAX (5 or 10 mg for three years or 20 mg for two years) followed by 5 mg for one year). There was a statistically significant reduction in the proportion of patients treated with FOSAMAX experiencing one or more new vertebral fractures relative to those treated with placebo (3.2% vs. 6.2%, a 48% relative risk reduction). A reduction in the total number of new vertebral fractures (4.2 vs. 11.3 per 100 patients) was also observed. In the pooled analysis, patients who received FOSAMAX had a loss in stature that was statistically significantly less than was observed in those who received placebo (-3.0 mm vs. -4.6 mm).
The Fracture Intervention Trial (FIT) consisted of two studies in postmenopausal women: the Three-Year Study of patients who had at least one baseline radiographic vertebral fracture and the Four-Year Study of patients with low bone mass but without a baseline vertebral fracture. In both studies of FIT, 96% of randomized patients completed the studies (i.e., had a closeout visit at the scheduled end of the study); approximately 80% of patients were still taking study medication upon completion.
Fracture Intervention Trial: Three-Year Study (patients with at least one baseline radiographic vertebral fracture)
This randomized, double-blind, placebo-controlled, 2027-patient study (FOSAMAX, n=1022; placebo, n=1005) demonstrated that treatment with FOSAMAX resulted in statistically significant reductions in fracture incidence at three years as shown in the table below.

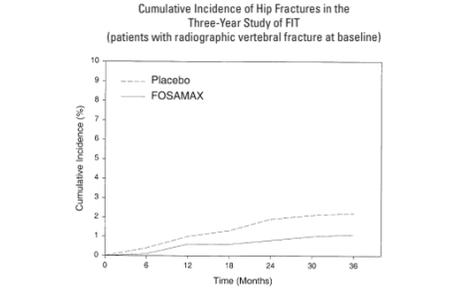
	Effect of FOSAMAX on Fracture Incidence in the Three-Year Study of FIT (patients with vertebral fracture at baseline)			
	Percent of Patients		Absolute Reduction in Fracture Incidence	Relative Reduction in Fracture Risk (%)
Patients with:	FOSAMAX (n=1022)	Placebo (n=1005)		
Vertebral fractures (diagnosed by X-ray) [†]				
≥ 1 new vertebral fracture	7.9	15.0	7.1	47***
≥ 2 new vertebral fractures	0.5	4.9	4.4	90***
Clinical (symptomatic) fractures				
Any clinical (symptomatic) fracture	13.8	18.1	4.3	26 [‡]
≥ 1 clinical (symptomatic) vertebral fracture	2.3	5.0	2.7	54**
Hip fracture	1.1	2.2	1.1	51*
Wrist (forearm) fracture	2.2	4.1	1.9	48*

[†]Number evaluable for vertebral fractures: FOSAMAX, n=984; placebo, n=966
*p<0.05, **p<0.01, ***p<0.001, [‡]p=0.007

Furthermore, in this population of patients with baseline vertebral fracture, treatment with FOSAMAX significantly reduced the incidence of hospitalizations (25.0% vs. 30.7%).

In the Three-Year Study of FIT, fractures of the hip occurred in 22 (2.2%) of 1005 patients on placebo and 11 (1.1%) of 1022 patients on FOSAMAX, p=0.047. The figure below displays the cumulative incidence of hip fractures in this study.

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Fracture Intervention Trial: Four-Year Study (patients with low bone mass but without a baseline radiographic vertebral fracture)
This randomized, double-blind, placebo-controlled, 4432-patient study (FOSAMAX, n=2214; placebo, n=2218) further investigated the reduction in fracture incidence due to FOSAMAX. The intent of the study was to recruit women with osteoporosis,

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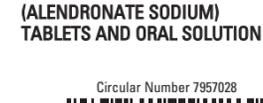
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defined as a baseline femoral neck BMD at least two standard deviations below the mean for young adult women. However, due to subsequent revisions to the normative values for femoral neck BMD, 31% of patients were found not to meet this entry criterion and thus this study included both osteoporotic and non-osteoporotic women. The results are shown in the table below for the patients with osteoporosis.

	Effect of FOSAMAX on Fracture Incidence in Osteoporotic [†] Patients in the Four-Year Study of FIT (patients without vertebral fracture at baseline)			
	Percent of Patients		Absolute Reduction in Fracture Incidence	Relative Reduction in Fracture Risk (%)
Patients with:	FOSAMAX (n=1545)	Placebo (n=1521)		
Vertebral fractures (diagnosed by X-ray) ^{††}				
≥ 1 new vertebral fracture	2.5	4.8	2.3	48***
≥ 2 new vertebral fractures	0.1	0.6	0.5	78*
Clinical (symptomatic) fractures				
Any clinical (symptomatic) fracture	12.9	16.2	3.3	22**
≥ 1 clinical (symptomatic) vertebral fracture	1.0	1.6	0.6	41 (NS) ^{†††}
Hip fracture	1.0	1.4	0.4	29 (NS) ^{†††}
Wrist (forearm) fracture	3.9	3.8	-0.1	NS ^{†††}

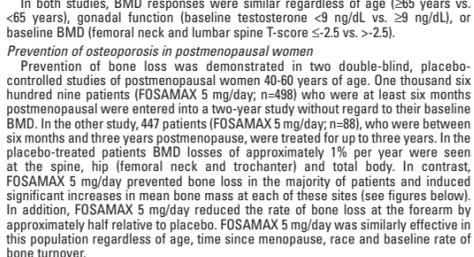
[†]Baseline femoral neck BMD at least 2 SD below the mean for young adult women
^{††}Number evaluable for vertebral fractures: FOSAMAX, n=1426; placebo, n=1428
^{†††}Not significant. This study was not powered to detect differences at these sites.
*p<0.035, **p<0.01, ***p<0.001

Fracture results across studies
In the Three-Year Study of FIT, FOSAMAX reduced the percentage of women experiencing at least one new radiographic vertebral fracture from 15.0% to 7.9% (47% relative risk reduction, p<0.001); in the Four-Year Study of FIT, the percentage was reduced from 3.8% to 2.1% (44% relative risk reduction, p=0.001); and in the combined U.S./Multinational studies, from 6.2% to 3.2% (48% relative risk reduction, p=0.034).
FOSAMAX reduced the percentage of women experiencing multiple (two or more) new vertebral fractures from 4.2% to 0.6% (87% relative risk reduction, p<0.001) in the combined U.S./Multinational studies and from 4.9% to 0.5% (89% relative risk reduction, p<0.001) in the Three-Year Study of FIT. In the Four-Year Study of FIT, FOSAMAX reduced the percentage of osteoporotic women experiencing multiple vertebral fractures from 0.6% to 0.1% (78% relative risk reduction, p=0.035).

Thus, FOSAMAX reduced the incidence of radiographic vertebral fractures in osteoporotic women whether or not they had a previous radiographic vertebral fracture.
FOSAMAX, over a three- or four-year period, was associated with statistically significant reductions in loss of height vs. placebo in patients with and without baseline radiographic vertebral fractures. At the end of the FIT studies the between-treatment group differences were 3.2 mm in the Three-Year Study and 1.3 mm in the Four-Year Study.
Bone histology
Bone histology in 270 postmenopausal patients with osteoporosis treated with FOSAMAX at doses ranging from 1 to 20 mg/day for one, two, or three years revealed normal mineralization and structure, as well as the expected decrease in bone turnover relative to placebo. These data, together with the normal bone histology and increased bone strength observed in rats and baboons exposed to long-term alendronate treatment, support the conclusion that bone formed during therapy with FOSAMAX is of normal quality.

Men
The efficacy of FOSAMAX in men with hypogonadal or idiopathic osteoporosis was demonstrated in two clinical studies.
A two-year, double-blind, placebo-controlled, multicenter study of FOSAMAX 10 mg once daily enrolled a total of 241 men between the ages of 31 and 87 (mean, 63). All patients in the trial had either: 1) a BMD T-score ≤-2 at the femoral neck and ≤-1 at the lumbar spine, or 2) a baseline osteoporotic fracture and a BMD T-score ≤-1 at the femoral neck. At two years, the mean increases relative to placebo in BMD in men receiving FOSAMAX 10 mg/day were significant at the following sites: lumbar spine, 5.3%; femoral neck, 2.6%; trochanter, 3.1%; and total body, 1.6%. Treatment with FOSAMAX also reduced height loss (FOSAMAX, -0.6 mm vs. placebo, -2.4 mm).
A one-year, double-blind, placebo-controlled, multicenter study of once weekly FOSAMAX 70 mg enrolled a total of 167 men between the ages of 38 and 91 (mean, 66). Patients in the study had either: 1) a BMD T-score ≤-2 at the femoral neck and ≤-1 at the lumbar spine, 2) a BMD T-score ≤-2 at the lumbar spine and ≤-1 at the femoral neck, or 3) a baseline osteoporotic fracture and a BMD T-score ≤-1 at the femoral neck. At one year, the mean increases relative to placebo in BMD in men receiving FOSAMAX 70 mg once weekly were significant at the following sites: lumbar spine, 2.8%; femoral neck, 1.9%; trochanter, 2.0%, and total body, 1.2%. These increases in BMD were similar to those seen at one year in the 10 mg once-daily study.

In both studies, BMD responses were similar regardless of age (<65 years vs. <65 years), gonadal function (baseline testosterone <9 ng/dL vs. ≥9 ng/dL), or baseline BMD (femoral neck and lumbar spine T-score ≤-2.5 vs. >-2.5).
Prevention of osteoporosis in postmenopausal women
Prevention of bone loss was demonstrated in two double-blind, placebo-controlled studies of postmenopausal women 40-60 years of age. One thousand six hundred nine patients (FOSAMAX 5 mg/day, n=498) who were at least six months postmenopausal were entered into a two-year study without regard to their baseline BMD. In the other study, 447 patients (FOSAMAX 5 mg/day, n=88), who were between six months and three years postmenopause, were treated for up to three years. In the placebo-treated patients BMD losses of approximately 1% per year were seen at the spine, hip (femoral neck and trochanter) and total body. In contrast, FOSAMAX 5 mg/day prevented bone loss in the majority of patients and induced significant increases in mean bone mass at each of these sites (see figures below). In addition, FOSAMAX 5 mg/day reduced the rate of bone loss at the forearm by approximately half relative to placebo. FOSAMAX 5 mg/day was similarly effective in this population regardless of age, time since menopause, race and baseline rate of bone turnover.



The therapeutic equivalence of once weekly FOSAMAX 35 mg (n=362) and FOSAMAX 5 mg daily (n=361) was demonstrated in a one-year, double-blind, multicenter study of postmenopausal women without osteoporosis. In the primary analysis of completers, the mean increases from baseline in lumbar spine BMD at one year were 2.9% (2.6, 3.2%; 95% CI) in the 35-mg once-weekly group (n=307) and 3.2% (2.9, 3.5%; 95% CI) in the 5-mg daily group (n=298). The two treatment groups were

Indications and Usage

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Bone histology was evaluated in 33 patients with Paget’s disease treated with FOSAMAX 40 mg/day for 6 months. As in patients treated for osteoporosis (see *Clinical Studies, Treatment of osteoporosis in postmenopausal women, Bone histology*), FOSAMAX did not impair mineralization, and the expected decrease in the rate of bone turnover was observed. Normal lamellar bone was produced during treatment with FOSAMAX, even where preexisting bone was woven and disorganized. Overall, bone histology data support the conclusion that bone formed during treatment with FOSAMAX is of normal quality.

ANIMAL PHARMACOLOGY

The relative inhibitory activities on bone resorption and mineralization of alendronate and etidronate were compared in the Schenk assay, which is based on histological examination of the epiphyses of growing rats. In this assay, the lowest dose of alendronate that interfered with bone mineralization (leading to osteomalacia) was 6000-fold the antiresorptive dose. The corresponding ratio for etidronate was one to one. These data suggest that alendronate administered in therapeutic doses is highly unlikely to induce osteomalacia.

INDICATIONS AND USAGE

FOSAMAX is indicated for:

- Treatment and prevention of osteoporosis in postmenopausal women
- For the treatment of osteoporosis, FOSAMAX increases bone mass and reduces the incidence of fractures, including those of the hip and spine (vertebral compression fractures). Osteoporosis may be confirmed by the finding of low bone mass (for example, at least 2 standard deviations below the premenopausal mean) or by the presence of a history of osteoporotic fracture. (See CLINICAL PHARMACOLOGY, *Pharmacodynamics*.)
- For the prevention of osteoporosis, FOSAMAX may be considered in postmenopausal women who are at risk of developing osteoporosis and for whom the desired clinical outcome is to maintain bone mass and to reduce the risk of future fracture. Bone loss is particularly rapid in postmenopausal women younger than age 60. Risk factors often associated with the development of postmenopausal osteoporosis include early menopause; moderately low bone mass (for example, at least 1 standard deviation below the mean for healthy young adult women); thin body build; Caucasian or Asian race; and family history of osteoporosis. The presence of such risk factors may be important when considering the use of FOSAMAX for prevention of osteoporosis.
- Treatment to increase bone mass in men with osteoporosis
- 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 (see PRECAUTIONS, *Glucocorticoid-induced osteoporosis*). Patients treated with glucocorticoids should receive adequate amounts of calcium and vitamin D.
- Treatment of Paget’s disease of bone in men and women
- Treatment is indicated in patients with Paget’s disease of bone having alkaline phosphatase at least two times the upper limit of normal, or those who are symptomatic, or those at risk for urine complications from their disease.

CONTRAINDICATIONS

- Abnormalities of the esophagus which delay esophageal emptying such as stricture or achalasia
- Inability to stand or sit upright for at least 30 minutes
- Patients at increased risk of aspiration should not receive FOSAMAX oral solution.
- Hypersensitivity to any component of this product
- Hypocalcemia (see PRECAUTIONS, *General*)

WARNINGS

FOSAMAX, like other bisphosphonates, may cause local irritation of the upper gastrointestinal mucosa.

Esophageal adverse experiences, such as esophagitis, esophageal ulcers and esophageal erosions, occasionally with bleeding and rarely followed by esophageal stricture or perforation, have been reported in patients receiving treatment with FOSAMAX. In some cases these have been severe and required hospitalization. Physicians should therefore be alert to any signs or symptoms signaling a possible esophageal reaction and patients should be instructed to discontinue FOSAMAX and seek medical attention if they develop dysphagia, odynophagia, retrosternal pain or new or worsening heartburn.

The risk of severe esophageal adverse experiences appears to be greater in patients who lie down after taking FOSAMAX and/or who fail to swallow it with the recommended amount of water, and/or who continue to take FOSAMAX after developing symptoms suggestive of esophageal irritation. Therefore, it is very important that the full dosing instructions are provided to, and understood by, the patient (see DOSAGE AND ADMINISTRATION). In patients who cannot comply with dosing instructions due to mental disability, therapy with FOSAMAX should be used under appropriate supervision.

Because of possible irritant effects of FOSAMAX on the upper gastrointestinal mucosa and a potential for worsening of the underlying disease, caution should be used when FOSAMAX is given to patients with active upper gastrointestinal problems (such as dysphagia, esophageal diseases, gastritis, duodenitis, or ulcers).

There have been post-marketing reports of gastric and duodenal ulcers, some severe and with complications, although no increased risk was observed in controlled clinical trials.

PRECAUTIONS

General

Causes of osteoporosis other than estrogen deficiency, aging, and glucocorticoid use should be considered.

Hypocalcemia must be corrected before initiating therapy with FOSAMAX (see CONTRAINDICATIONS). Other disorders affecting mineral metabolism (such as vitamin D deficiency) should also be effectively treated. In patients with these conditions, serum calcium and symptoms of hypocalcemia should be monitored during therapy with FOSAMAX.

Presumably due to the effects of FOSAMAX on increasing bone mineral, small, asymptomatic decreases in serum calcium and phosphate may occur, especially in patients with Paget’s disease, in whom the pretreatment rate of bone turnover may be greatly elevated and in patients receiving glucocorticoids, in whom calcium absorption may be decreased.

Ensuring adequate calcium and vitamin D intake is especially important in patients with Paget’s disease of bone and in patients receiving glucocorticoids.

Musculoskeletal Pain

In post marketing experience, severe and occasionally incapacitating bone, joint, and/or muscle pain has been reported in patients taking bisphosphonates that are approved for the prevention and treatment of osteoporosis (see ADVERSE REACTIONS). However, such reports have been infrequent. This category of drugs includes FOSAMAX (alendronate). Most of the patients were postmenopausal women. The time to onset of symptoms varied from one day to several months after starting the drug. Most patients had relief of symptoms after stopping. A subset had recurrence of symptoms when rechallenged with the same drug or another bisphosphonate.

In placebo-controlled clinical studies of FOSAMAX, the percentages of patients with these symptoms were similar in the FOSAMAX and placebo groups.

Dental

Osteonecrosis of the jaw, generally associated with tooth extraction and/or local infection, often with delayed healing, has been reported in patients taking bisphosphonates. Most reported cases of bisphosphonate-associated osteonecrosis have been in cancer patients treated with intravenous bisphosphonates, but some have occurred in patients with postmenopausal osteoporosis. Known risk factors for osteonecrosis include a diagnosis of cancer, concomitant therapies (e.g., chemotherapy, radiotherapy, corticosteroids), poor oral hygiene, and co-morbid disorders (e.g., pre-existing dental disease, anemia, coagulopathy, infection).

Patients who develop osteonecrosis of the jaw (ONJ) while on bisphosphonate therapy should receive care by an oral surgeon. Dental surgery may exacerbate the condition. For patients requiring dental procedures, there are no data available to suggest whether discontinuation of bisphosphonate treatment reduces the risk for ONJ. Clinical judgment of the treating physician should guide the management plan of each patient based on individual benefit/risk assessment.

Adverse Experiences

Pharmacokinetics

Pharmacology and Toxicology

Preclinical Toxicology

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Patient Information
FOSAMAX® (alendronate sodium) Tablets

Read this information before you start taking FOSAMAX* (FOSS-ah-max). Also, read the leaflet each time you refill your prescription, just in case anything has changed. This leaflet does not take the place of discussions with your doctor. You and your doctor should discuss FOSAMAX when you start taking your medicine and at regular checkups.

What is the most important information I should know about FOSAMAX?

- **You must take FOSAMAX exactly as directed to help make sure it works and to help lower the chance of harmful side effects.**
- **After getting up for the day and before taking your first food, drink, or other medicine, swallow your FOSAMAX tablet with a full glass (6-8 oz) of plain water only.**
 - **Not** mineral water
 - **Not** coffee or tea
 - **Not** juice
- **Do not chew or suck on a tablet of FOSAMAX.**
- **After swallowing your FOSAMAX tablet, do not lie down – stay fully upright (sitting, standing, or walking) for at least 30 minutes. Do not lie down until after your first food of the day.** This will help the FOSAMAX tablet reach your stomach quickly and help reduce the chance that FOSAMAX might irritate your esophagus, the tube that connects your mouth with your stomach.
- **After swallowing your FOSAMAX tablet, wait at least 30 minutes before taking your first food, drink, or other medicine of the day,** including antacids, calcium, and other supplements and vitamins. FOSAMAX is effective only if it is taken when your stomach is empty.
- **Do not take FOSAMAX at bedtime or before getting up for the day.**
- **If you have chest pain, new or worsening heartburn, or have trouble or pain when you swallow, stop taking FOSAMAX and call your doctor.**

What is FOSAMAX?

FOSAMAX is for:

- The treatment or prevention of osteoporosis (thinning of bone) in women after menopause. It reduces the chance of having a hip or spinal fracture (break).
- Treatment to increase bone mass in men with osteoporosis.
- The treatment of osteoporosis in either men or women receiving corticosteroid medicines (for example, prednisone).

Improvement in bone density may be seen as early as 3 months after you start taking FOSAMAX. For FOSAMAX to continue to work, you need to keep taking it.

FOSAMAX is not a hormone.

There is more information about osteoporosis at the end of this leaflet.

Who should not take FOSAMAX?

Do not take FOSAMAX if you:

- Have certain problems with your esophagus, the tube that connects your mouth with your stomach
- Cannot stand or sit upright for at least 30 minutes
- Have low levels of calcium in your blood
- Have severe kidney disease
- Are allergic to FOSAMAX or any of its ingredients. A list of ingredients is at the end of this leaflet.

If you are pregnant or nursing, talk to your doctor about whether taking FOSAMAX is right for you based on possible risk to you and your child.

Talk to your doctor about any:

- Problems with swallowing
- Stomach or digestive problems
- Other medical problems you have or have had in the past
- Medicines you take, including prescription and non-prescription medicines, vitamins, and herbal supplements

How should I take FOSAMAX?

See "What is the most important information I should know about FOSAMAX?" for important information about how to take the medicine and to help make sure it works for you. In addition, follow these instructions:

- After getting up for the day and before taking your first food, drink, or other medicine, swallow your FOSAMAX tablet with a full glass (6-8 oz) of plain water only.
- Take 1 FOSAMAX tablet once a day, every day.
- It is important that you keep taking FOSAMAX for as long as your doctor says to take it. For FOSAMAX to continue to work, you need to keep taking it.
- If you miss a dose, do not take it later in the day. Continue your usual schedule of 1 tablet once a day the next morning.
- If you think you took more than the prescribed dose of FOSAMAX, drink a full glass of milk and contact your local poison control center or emergency room right away. Do not try to vomit. Do not lie down.

What should I avoid while taking FOSAMAX?

- **Do not eat, drink, or take other medicines or supplements before taking FOSAMAX.**
- **Wait for at least 30 minutes after taking FOSAMAX to eat, drink, or take other medicines or supplements.**
- **Do not lie down for at least 30 minutes after taking FOSAMAX. Do not lie down until after your first food of the day.**

What are the possible side effects of FOSAMAX?

Some patients may get severe digestive reactions from FOSAMAX. (See "What is the most important information I should know about FOSAMAX?") These reactions include irritation, inflammation, or ulcers of the esophagus, which may sometimes bleed. This may occur especially if patients do not drink a full glass of water with FOSAMAX or if they lie down in less than 30 minutes or before their first food of the day. Esophagus reactions may get worse if patients continue to take FOSAMAX after developing symptoms of an irritated esophagus.

Stop taking FOSAMAX and call your doctor right away if you get any of these signs of possible serious problems:

- Chest pain
- Heartburn
- Trouble or pain when swallowing

Side effects in patients taking FOSAMAX usually have been mild. They generally have not caused patients to stop taking FOSAMAX.

The most common side effect is abdominal (stomach area) pain. Less common side effects are nausea, vomiting, a full or bloated feeling in the stomach, constipation, diarrhea, black or bloody stools (bowel movements), gas, headache, a changed sense of taste, and bone, muscle, and/or joint pain.

FOSAMAX®
(alendronate sodium)
Tablets

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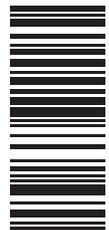
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FOSAMAX® (alendronate sodium) Tablets

Severe bone, joint, and/or muscle pain has been reported in patients taking, by mouth, bisphosphonates drugs that are used to treat osteoporosis (thin bones). However, such reports have been rare. This group of drugs includes FOSAMAX. Most of the patients were postmenopausal women (women who had stopped having periods). Patients developed pain within one day to several months after starting the drug. Most patients experienced relief after stopping the drug. Patients who develop severe bone, joint, and/or muscle pain after starting FOSAMAX should contact their physician.

Transient flu-like symptoms (rarely with fever), typically at the start of treatment, have occurred.

In rare cases, patients taking FOSAMAX may get itching or eye pain, or a rash that may be made worse by sunlight. Rarely, severe skin reactions may occur. Patients may get allergic reactions, such as hives or, in rare cases, swelling that can be of their face, lips, tongue, or throat, which may cause trouble in breathing or swallowing. Mouth ulcers (sores) may occur if FOSAMAX is chewed or dissolved in the mouth.

Rarely, patients have had jaw problems associated with delayed healing and infection, often following tooth extraction.

Anytime you have a medical problem you think may be from FOSAMAX, talk to your doctor.

What should I know about osteoporosis?

Normally your bones are being rebuilt all the time. First, old bone is removed (resorbed). Then a similar amount of new bone is formed. This balanced process keeps your skeleton healthy and strong.

Osteoporosis is a thinning and weakening of the bones. It is common in women after menopause, and may also occur in men. In osteoporosis, bone is removed faster than it is formed, so overall bone mass is lost and bones become weaker. Therefore, keeping bone mass is important to keep your bones healthy. In both men and women, osteoporosis may also be caused by certain medicines called corticosteroids.

At first, osteoporosis usually has no symptoms, but it can cause fractures (broken bones). Fractures usually cause pain. Fractures of the bones of the spine may not be painful, but over time they can make you shorter. Eventually, your spine can curve and your body can become bent over. Fractures may happen during normal, everyday activity, such as lifting, or from minor injury that would normally not cause bones to break. Fractures most often occur at the hip, spine, or wrist. This can lead to pain, severe disability, or loss of ability to move around (mobility).

Who is at risk for osteoporosis?

Many things put people at risk of osteoporosis. The following people have a higher chance of getting osteoporosis:

Women who:

- Are going through or who are past menopause

Men who:

- Are elderly

People who:

- Are white (Caucasian) or oriental (Asian)
- Are thin
- Have family member with osteoporosis
- Do not get enough calcium or vitamin D

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FOSAMAX® (alendronate sodium) Tablets

- Do not exercise
- Smoke
- Drink alcohol often
- Take bone thinning medicines (like prednisone or other corticosteroids) for a long time

What can I do to help prevent or treat osteoporosis?

In addition to FOSAMAX, your doctor may suggest one or more of the following lifestyle changes:

- **Stop smoking.** Smoking may increase your chance of getting osteoporosis.
- **Reduce the use of alcohol.** Too much alcohol may increase the risk of osteoporosis and injuries that can cause fractures.
- **Exercise regularly.** Like muscles, bones need exercise to stay strong and healthy. Exercise must be safe to prevent injuries, including fractures. Talk with your doctor before you begin any exercise program.
- **Eat a balanced diet.** Having enough calcium in your diet is important. Your doctor can advise you whether you need to change your diet or take any dietary supplements, such as calcium or vitamin D.

What are the ingredients in FOSAMAX?

FOSAMAX contains alendronate sodium as the active ingredient and the following inactive ingredients: cellulose, lactose, croscarmellose sodium and magnesium stearate. The 10 mg tablet also contains carnauba wax.

How do I store FOSAMAX?

Store FOSAMAX at room temperature, 59-86°F (15-30°C).

Discard all expired medicines. Keep all medicines out of the reach of children.

General information about using FOSAMAX safely and effectively

Medicines are sometimes prescribed for conditions that are not mentioned in patient information leaflets. This medicine was prescribed for your particular condition. FOSAMAX acts specifically on your bones. Do not use it for another condition or give it to others.

This leaflet is a summary of information about FOSAMAX. If you have any questions or concerns about FOSAMAX or osteoporosis, talk to your doctor, pharmacist, or other health care provider. You can ask your doctor or pharmacist for information about FOSAMAX written for health care providers. For more information, call 1-877-408-4699 (toll-free) or visit the following website: www.fosamax.com.

MERCK & CO., INC.
Whitehouse Station, NJ 08889, USA





Patient Information
Once Weekly FOSAMAX® (alendronate sodium)
Tablets and Oral Solution

Read this information before you start taking FOSAMAX® (FOSS-ah-max). Also, read the leaflet each time you refill your prescription, just in case anything has changed. This leaflet does not take the place of discussions with your doctor. You and your doctor should discuss FOSAMAX when you start taking your medicine and at regular checkups.

What is the most important information I should know about once weekly FOSAMAX?

- You must take once weekly FOSAMAX exactly as directed to help make sure it works and to help lower the chance of harmful side effects.
- Choose the day of the week that best fits your schedule. Every week, take 1 dose of FOSAMAX (one tablet or one entire bottle of solution) on your chosen day.
- After getting up for the day and before taking your first food, drink, or other medicine, take your FOSAMAX with plain water only as follows:
 - TABLETS: Swallow one tablet with a full glass (6-8 oz) of plain water.
 - ORAL SOLUTION: Drink one entire bottle of solution followed by at least 2 ounces (a quarter of a cup) of plain water.

Do not take FOSAMAX with:

Mineral water
Coffee or tea
Juice

- Do not chew or suck on a tablet of FOSAMAX.
- After taking your FOSAMAX, do not lie down – stay fully upright (sitting, standing, or walking) for at least 30 minutes. Do not lie down until after your first food of the day. This will help FOSAMAX reach your stomach quickly and help reduce the chance that FOSAMAX might irritate your esophagus, the tube that connects your mouth with your stomach.
- After taking your FOSAMAX, wait at least 30 minutes before taking your first food, drink, or other medicine of the day, including antacids, calcium, and other supplements and vitamins. FOSAMAX is effective only if it is taken when your stomach is empty.
- Do not take FOSAMAX at bedtime or before getting up for the day.
- If you have chest pain, new or worsening heartburn, or have trouble or pain when you swallow, stop taking FOSAMAX and call your doctor.

What is FOSAMAX?

FOSAMAX is for:

- The treatment or prevention of osteoporosis (thinning of bone) in women after menopause. It reduces the chance of having a hip or spinal fracture (break).
- Treatment to increase bone mass in men with osteoporosis.

FOSAMAX tablets are for treatment and prevention, and FOSAMAX oral solution is for treatment of osteoporosis.

Improvement in bone density may be seen as early as 3 months after you start taking FOSAMAX. For FOSAMAX to continue to work, you need to keep taking it.

FOSAMAX is not a hormone.

There is more information about osteoporosis at the end of this leaflet.

Who should not take FOSAMAX?

Do not take FOSAMAX (tablets or oral solution) if you:

- Have certain problems with your esophagus, the tube that connects your mouth with your stomach

- Cannot stand or sit upright for at least 30 minutes
- Have low levels of calcium in your blood
- Have severe kidney disease
- Are allergic to FOSAMAX or any of its ingredients. A list of ingredients is at the end of this leaflet.

Do not take FOSAMAX oral solution if you have difficulty swallowing liquids.

If you are pregnant or nursing, talk to your doctor about whether taking FOSAMAX is right for you based on possible risk to you and your child.

Talk to your doctor about any:

- Problems with swallowing
- Stomach or digestive problems
- Other medical problems you have or have had in the past
- Medicines you take, including prescription and non-prescription medicines, vitamins, and herbal supplements

How should I take once weekly FOSAMAX?

See "What is the most important information I should know about once weekly FOSAMAX?" for important information about how to take the medicine and to help make sure it works for you. In addition, follow these instructions:

- Take 1 dose of FOSAMAX once a week.
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 - TABLETS: Swallow one tablet with a full glass (6-8 oz) of plain water.
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- It is important that you keep taking FOSAMAX for as long as your doctor says to take it. For FOSAMAX to continue to work, you need to keep taking it.
- If you miss a dose, take only 1 dose of FOSAMAX on the morning after you remember. Do not take 2 doses on the same day. Continue your usual schedule of 1 dose once a week on your chosen day.
- If you think you took more than the prescribed dose of FOSAMAX, drink a full glass of milk and contact your local poison control center or emergency room right away. Do not try to vomit. Do not lie down.

What should I avoid while taking FOSAMAX?

- Do not eat, drink, or take other medicines or supplements before taking FOSAMAX.
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- Do not lie down for at least 30 minutes after taking FOSAMAX. Do not lie down until after your first food of the day.

What are the possible side effects of FOSAMAX?

Some patients may get severe digestive reactions from FOSAMAX. (See "What is the most important information I should know about once weekly FOSAMAX?") These reactions include irritation, inflammation, or ulcers of the esophagus, which may sometimes bleed. This may occur especially if patients do not drink the recommended amount of water with FOSAMAX or if they lie down in less than 30 minutes or before their first food of the day. Esophagus reactions may get worse if patients continue to take FOSAMAX after developing symptoms of an irritated esophagus.

Once Weekly
FOSAMAX®
 (alendronate sodium)
 Tablets and Oral Solution

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FOSAMAX® (alendronate sodium)
Tablets and Oral Solution

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Side effects in patients taking FOSAMAX usually have been mild. They generally have not caused patients to stop taking FOSAMAX.

The most common side effect is abdominal (stomach area) pain. Less common side effects are nausea, vomiting, a full or bloated feeling in the stomach, constipation, diarrhea, black or bloody stools (bowel movements), gas, headache, a changed sense of taste, and bone, muscle, and/or joint pain.

Severe bone, joint, and/or muscle pain has been reported in patients taking, by mouth, bisphosphonates drugs that are used to treat osteoporosis (thin bones). However, such reports have been rare. This group of drugs includes FOSAMAX. Most of the patients were postmenopausal women (women who had stopped having periods). Patients developed pain within one day to several months after starting the drug. Most patients experienced relief after stopping the drug. Patients who develop severe bone, joint, and/or muscle pain after starting FOSAMAX should contact their physician.

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Issued July 2005

FOSAMAX® (alendronate sodium)
Tablets and Oral Solution

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- Are going through or who are past menopause

Men who:

- Are elderly

People who:

- Are white (Caucasian) or oriental (Asian)
- Are thin
- Have family member with osteoporosis
- Do not get enough calcium or vitamin D
- Do not exercise
- Smoke
- Drink alcohol often
- Take bone thinning medicines (like prednisone or other corticosteroids) for a long time

What can I do to help prevent or treat osteoporosis?

In addition to FOSAMAX, your doctor may suggest one or more of the following lifestyle changes:

- **Stop smoking.** Smoking may increase your chance of getting osteoporosis.
- **Reduce the use of alcohol.** Too much alcohol may increase the risk of osteoporosis and injuries that can cause fractures.
- **Exercise regularly.** Like muscles, bones need exercise to stay strong and healthy. Exercise must be safe to prevent injuries, including fractures. Talk with your doctor before you begin any exercise program.
- **Eat a balanced diet.** Having enough calcium in your diet is important. Your doctor can advise you whether you need to change your diet or take any dietary supplements, such as calcium or vitamin D.

What are the ingredients in FOSAMAX?

Tablets

FOSAMAX tablets contain alendronate sodium as the active ingredient and the following inactive ingredients: cellulose, lactose, croscarmellose sodium and magnesium stearate.

Oral Solution

Fosamax oral solution contains alendronate sodium as the active ingredient and the following inactive ingredients: sodium citrate, citric acid, sodium saccharin, artificial raspberry flavor, purified water, sodium propylparaben and sodium butylparaben.

How do I store FOSAMAX?

Tablets

Store at room temperature, 59-86°F (15-30°C).

Oral Solution

Store at 77°F (25°C). Occasional storage between 59-86°F (15-30°C) is allowed. Do not freeze.

Discard all expired medicines. Keep all medicines out of the reach of children.

General information about using FOSAMAX safely and effectively

Medicines are sometimes prescribed for conditions that are not mentioned in patient information leaflets. This medicine was prescribed for your particular condition. FOSAMAX acts specifically on your bones. Do not use it for another condition or give it to others.

This leaflet is a summary of information about FOSAMAX. If you have any questions or concerns about FOSAMAX or osteoporosis, talk to your doctor, pharmacist, or other health care provider. You can ask your doctor or pharmacist for information about FOSAMAX written for health care providers. For more information, call 1-877-408-4699 (toll-free) or visit the following website: www.fosamax.com.

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