

NEW ZEALAND DATA SHEET

AURO-ALENDRONATE

Alendronate as sodium alendronate

70 mg tablet

This product may not be interchangeable with similar products on the New Zealand market.

PRESENTATION

White to off-white, oval shaped, biconvex, uncoated tablets debossed with 'F' on one side and '21' on the other side.

USES

Actions

Bisphosphonates are synthetic analogs of pyrophosphate that bind to the hydroxyapatite found in bone. Alendronate is a bisphosphonate that acts as a potent, specific inhibitor of osteoclast-mediated bone resorption.

Animal studies have indicated the following mode of action. At the cellular level, alendronate shows preferential localisation 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 localisation 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 where it is no longer 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. number of sites at which bone is remodelled). In addition bone formation exceeds bone resorption at these remodelling 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 standardised breakfast. Oral bioavailability in men (0.6%) was similar to that in women. Bioavailability was decreased similarly (by approximately 40%) whether alendronate was administered one or one-half hour before a standardised breakfast. In osteoporosis and Paget's disease studies, alendronate was effective when administered at least 30 minutes before the first food or beverage of the day.

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Bioavailability was negligible whether alendronate was administered with or up to two hours after a standardised breakfast. Concomitant administration of alendronate with coffee or orange juice reduced bioavailability by approximately 60%.

In healthy subjects, oral prednisone (20 mg three times daily for 5 days) did not produce a clinically meaningful change in the oral bioavailability of alendronate (a mean increase ranging 20 to 44 %).

The oral bioavailability in children (4 to 16 years of age) with osteogenesis imperfecta (OI) was similar to that observed in adults (see **Paediatric Use**).

Distribution

Studies in 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 medicine in plasma following therapeutic oral doses are too low for analytical detection (less than 5 ng/mL). Protein binding in human plasma is approximately 78%.

Biotransformation or Metabolism

There is no evidence that alendronate is metabolised in animals or humans.

Elimination

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 faeces. Following a single 10 mg IV dose, the renal clearance of alendronate was 71 mL/min, 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, reflecting the release of alendronate from the skeleton.

Characteristics in Patients

Preclinical studies show that the medicine that is not deposited in bone is rapidly excreted in the urine. No evidence of saturation of bone uptake was found after chronic dosing with cumulative IV doses up to 35 mg/kg in animals. 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 accumulation of alendronate in bone might be expected in patients with impaired renal function (see **Dosage and Administration**).

Indications

Auro-Alendronate is indicated:

- In postmenopausal women for the treatment of osteoporosis to prevent fractures, including those of the hip and spine (vertebral compression fractures).
- For the treatment of osteoporosis in men to prevent fractures.

DOSAGE AND ADMINISTRATION

Auro-Alendronate must be taken at least one half hour before the first food, beverage, or medication of the day with plain water only. Other beverages (including mineral water), food, and some medications are likely to reduce the absorption of alendronate (see **Interactions**). Tablets are not to be divided.

To facilitate delivery to the stomach and thus reduce the potential for oesophageal irritation, Auro-Alendronate should only be swallowed upon arising for the day with a full glass of water and patients should not lie down for at least 30 minutes and until after their first food of the day. Auro-Alendronate should not be taken at bedtime or before arising for the day. Failure to follow these instructions may increase the risk of oesophageal adverse experiences (see **Warnings and Precautions**).

Patients should receive supplemental calcium and vitamin D, if dietary calcium is inadequate (see **Warnings and Precautions**).

No dosage adjustment is necessary for the elderly or for patients with mild-to-moderate renal insufficiency (creatinine clearance 35 to 60 mL/min). Auro-Alendronate is not recommended for patients with more severe renal insufficiency (creatinine clearance <35 mL/min) due to lack of experience.

Treatment of Osteoporosis in Postmenopausal Women and in Men

The recommended dosage is one 70 mg tablet once weekly.

CONTRAINDICATIONS

- Abnormalities of the oesophagus which delay oesophageal emptying such as stricture or achalasia.
- Inability to stand or sit upright for at least 30 minutes.
- Hypersensitivity to any component of this product.
- Hypocalcaemia (see **Warnings and Precautions**).

WARNINGS AND PRECAUTIONS

SEVERE OESOPHAGEAL ULCERATION HAS BEEN REPORTED IN PATIENTS TAKING ALENDRONATE. SEE DOSAGE AND ADMINISTRATION. PHYSICIANS SHOULD THEREFORE BE ALERT TO ANY SIGNS OR SYMPTOMS SIGNALING A POSSIBLE OESOPHAGEAL REACTION. PATIENTS SHOULD BE INSTRUCTED TO DISCONTINUE AURO-ALENDRONATE AND SEEK MEDICAL ATTENTION IF THEY DEVELOP DYSPHAGIA, ODYNOPHAGIA OR RETROSTERNAL PAIN.

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

Oesophageal adverse experiences, such as oesophagitis, oesophageal ulcers and oesophageal erosions, rarely followed by oesophageal stricture or perforation have been reported in patients receiving treatment with alendronate. In some cases these have been severe and required hospitalisation.

The risk of severe oesophageal adverse experiences appears to be greater in patients who lie down after taking alendronate and/or who fail to swallow it with the recommended amount of water, and/or who continue to take alendronate after developing symptoms suggestive of oesophageal irritation. Therefore, it is very important that the full dosing instructions are provided to, and understood by, the patient (see **Dosage and Administration**).

While no increased risk was observed in extensive clinical trials, there have been rare (post-marketing) reports of gastric and duodenal ulcers, some severe and with complications.

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

Causes of osteoporosis other than oestrogen deficiency, ageing, and glucocorticoid use should be considered.

Hypocalcaemia must be corrected before initiating therapy with alendronate (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 hypocalcaemia should be monitored during therapy with alendronate.

Due to the positive effects of alendronate in increasing bone mineral, small, asymptomatic decreases in serum calcium and phosphate may occur, especially in patients with Paget's disease, in whom the pre-treatment 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.

Dental

Localised osteonecrosis of the jaw (ONJ), generally associated with tooth extraction and/or local infection (including osteomyelitis) with delayed healing, has been reported rarely with oral bisphosphonates (see **Adverse Effects**, Post-Marketing Experience). Most reported cases of bisphosphonate-associated ONJ have been in cancer patients treated with intravenous bisphosphonates. Known risk factors for ONJ include a diagnosis of cancer, concomitant therapies (e.g., chemotherapy, radiotherapy, corticosteroids), poor oral hygiene, co-morbid disorders (e.g., periodontal and/or other pre-existing dental disease, anaemia, coagulopathy, infection) and smoking. In patients who develop ONJ while on bisphosphonate therapy, the clinical judgment of the treating physician should guide the management plan to include appropriate care by an oral surgeon and discontinuation of bisphosphonate therapy should be considered based on individual benefit/risk assessment. Dental surgery may exacerbate the condition.

Prior to treatment with bisphosphonates, a dental examination with appropriate preventative dentistry should be considered in patients with possible risk factors.

For patients requiring invasive dental surgery (e.g., tooth extraction, dental implants), there are no definitive data available to establish whether discontinuation of bisphosphonate treatment reduces the risk of ONJ. Therefore clinical judgment of the treating physician and/or oral surgeon should guide the management plan, including discontinuation of bisphosphonate treatment, of each patient based on individual benefit/risk assessment.

Musculoskeletal Pain

Bone, joint, and/or muscle pain has been reported in patients taking bisphosphonates. In post-marketing experience, these symptoms have rarely been severe and/or incapacitating (see **Adverse Effects**, Post-Marketing Experience). The time to onset of symptoms varied from one day to several months after starting treatment. Most patients had relief of symptoms after stopping treatment. A subset had recurrence of symptoms when rechallenged with the same medicine or another bisphosphonate.

Atypical Stress Fractures

A small number of long-term (usually longer than three years) alendronate-treated patients developed stress fractures of the proximal femoral shaft (also known as insufficiency fractures), some of which occurred in the absence of apparent trauma. Some patients experienced prodromal pain in the affected area, often associated with imaging features of stress fracture, weeks to months before a complete fracture occurred. Approximately one third of these fractures were bilateral; therefore the contralateral femur should be examined in patients who have sustained a femoral shaft stress fracture. The number of reported cases of this condition is very low (some 40 reported cases world-wide). Patients with suspected stress fractures should be evaluated, including evaluation for known causes and risk factors (e.g., vitamin D deficiency, malabsorption, glucocorticoid use, previous stress fracture, lower extremity arthritis or fracture, extreme or increased exercise, diabetes mellitus, chronic alcohol abuse), and receive appropriate orthopaedic care. Discontinuation of bisphosphonate therapy in patients with stress fractures is advisable pending evaluation of the patient, based on individual benefit/risk assessment. A cause and effect relationship between bisphosphonate use and stress fractures has not been excluded.

Renal Insufficiency

Alendronate is not recommended for patients with creatinine clearance <35 mL/min (see **Dosage and Administration**).

Nephrolithiasis and Hypercalciuria

Patients with a history of either nephrolithiasis or hypercalciuria may require special diets that limit their calcium intake. The calcium content of BoneCal should be considered when these diets are prescribed.

Dosing Instructions for Patients

To facilitate delivery to the stomach and thus reduce the potential for oesophageal irritation patients should be instructed to swallow Auro-Alendronate tablet with a full glass of water and not to lie down for at least 30 minutes and until after their first food of the day. Patients should not chew or suck on the tablet because of a potential for oropharyngeal ulceration.

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Patients should be specifically instructed not to take Auro-Alendronate tablet at bedtime or before arising for the day. Patients should be informed that failure to follow these instructions may increase their risk of oesophageal problems. Patients should be instructed that if they develop symptoms of oesophageal disease (such as difficulty or pain upon swallowing, retrosternal pain or new or worsening heartburn) they should stop taking alendronate and consult their physician.

Patients should be instructed that if they miss a dose of Auro-Alendronate once weekly, they should take one tablet on the morning after they remember. They should not take two tablets on the same day but should return to taking one tablet once a week, as originally scheduled on their chosen day.

Pregnancy (Category B3)

Alendronate has not been studied in pregnant women and should not be given to them. In studies with pregnant rats, oral alendronate doses of 2 mg/kg/day and above resulted in dystocia due to maternal hypocalcaemia. Foetal weight was reduced in rats at maternal doses greater than 5 mg/kg/day. No teratogenic effects were seen in rats or rabbits at oral doses up to 25 and 35 mg/kg/day, respectively.

Nursing Mothers

Alendronate has not been studied in breast-feeding women and should not be given to them.

Paediatric use

Alendronate is not indicated for use in children.

Use in Elderly

In clinical studies, there was no age-related difference in the efficacy or safety profiles of alendronate.

Effects on ability to drive and use machinery

No studies on the effects on the ability to drive and use machines have been performed. However, certain adverse reactions that have been reported with alendronate may affect some patients' ability to drive or operate machinery. Individual responses to alendronate may vary (see **Adverse Effects**).

Laboratory Test Findings

In double-blind, multicentre, controlled studies, asymptomatic, mild and transient decreases in serum calcium and phosphate were observed in approximately 18 and 10%, respectively, of patients taking alendronate versus approximately 12 and 3% of those taking placebo. However, the incidences of decreases in serum calcium to <8.0 mg/dL (2.0 mM) and serum phosphate to <2.0 mgP/dL (0.65 mM) were similar in both treatment groups.

Animal Toxicology

Carcinogenicity

No evidence of carcinogenic effect was observed in a 105-week study in rats receiving oral doses up to 3.75 mg/kg/day and in a 92-week study in mice receiving oral doses up to 10 mg/kg/day.

Mutagenicity and Genotoxicity

Alendronate was not genotoxic in the *in vitro* microbial mutagenesis assay with and without metabolic activation. Similarly, no evidence of mutagenicity was observed in an *in vitro* mammalian cell mutagenesis assay, an *in vitro* alkaline elution assay in rat hepatocytes, and an *in vivo* chromosomal aberration assay in mice at IV doses up to 25 mg/kg/day (75 mg/m²).

In an *in vitro* chromosomal aberration assay in Chinese hamster ovary cells, however, alendronate was weakly positive at concentrations ≥ 5 mM in the presence of cytotoxicity. This is of no relevance to safety in humans since similar concentrations are not achievable *in vivo* at therapeutic doses. Furthermore, clear negative results in four of five genotoxicity studies, including the most relevant studies for human carcinogenic potential (the *in vivo* chromosomal aberration assay and the microbial mutagenesis assay), and negative carcinogenicity studies in rats and mice lead to the conclusion that there is no evidence of genotoxic or carcinogenic risks from alendronate in humans.

Reproduction

Alendronate had no effect on fertility or reproductive performance (male or female) in rats at oral doses up to 5 mg/kg/day. The only medicine-related effect seen in these studies was difficulty in parturition in rats, which is directly related to pharmacologically mediated hypocalcaemia. This effect can be prevented in rats by calcium supplementation. Furthermore, a clear no-effect level of 1.25 mg/kg/day was established.

Fertility

Alendronate sodium had no effect on fertility in male and female rats at oral doses of up to 9 and 15 mg/kg/day.

Development

In developmental toxicity studies, there were no adverse effects at doses up to 25 mg/kg/day in rats and 35 mg/kg/day in rabbits.

ADVERSE EFFECTS

Clinical studies

In clinical studies alendronate was generally well tolerated. In studies of up to 5 years in duration, adverse effects which usually were mild, generally did not require discontinuation of therapy.

Treatment of Osteoporosis

Postmenopausal Women

Alendronate has been evaluated for safety in clinical studies in approximately 5000 postmenopausal patients. In two three-year, placebo controlled, double blind multicentre studies, discontinuation of therapy due to any clinical adverse experience occurred in 4.1% of 196 patients treated with Alendronate 10 mg/day and 6.0% of 397 patients treated with placebo. Adverse experiences reported by the investigators as possibly, probably or definitely drug related in $\geq 1\%$ of patients treated with either Alendronate 10 mg/day or placebo are presented in the following table:

Drug Related Adverse Experiences Reported in $\geq 1\%$ of Patients		
	Alendronate 10 mg/day % (n=196)	Placebo % (n=196)
Gastrointestinal		
abdominal pain	6.6	4.8
nausea	3.6	4.0
dyspepsia	3.6	3.5
diarrhoea	3.1	1.8
constipation	3.1	1.8
flatulence	2.6	0.5
acid regurgitation	2.0	4.3
oesophageal ulcer	1.5	0.0
vomiting	1.0	1.5
dysphagia	1.0	0.0
abdominal distension	1.0	0.8
gastritis	0.5	1.3
Musculoskeletal		
musculoskeletal (bone, muscle or joint) pain	4.1	2.5
muscle cramp	0.0	1.0
Nervous System/Psychiatric		
headache	2.6	1.5
dizziness	0.0	1.0
Special Senses		
taste perversion	0.5	1.0
Rarely, rash and erythema have occurred.		

In the two-year extension (treatment years 4 and 5) of the above studies, the overall safety profile of alendronate 10 mg/day was similar to that observed during the three-year placebo-controlled period. Additionally, the proportion of patients who discontinued alendronate 10 mg/day due to any clinical adverse experience was similar to that during the first three years of the study.

In the Fracture Intervention Trial, discontinuation of therapy due to any clinical adverse experience occurred in 9.1% of 3236 patients treated with alendronate 5 mg/day for 2 years

and 10 mg/day for either one or two additional years and 10.1% of 3223 patients treated with placebo. Discontinuations due to upper gastrointestinal adverse experiences were: alendronate, 3.2%; placebo, 2.7%. The overall adverse experience profile was similar to that seen in other studies with alendronate 5 or 10 mg/day.

In a one year, double-blind, multicentre study, the overall safety and tolerability profiles of alendronate once weekly 70 mg (n=519) and alendronate 10 mg daily (n=370) were similar. The following adverse experiences were reported by the investigators as possibly, probably, or definitely medicine related in $\geq 1\%$ of patients in either treatment group are presented in the following table:

Drug Related Adverse Experiences Reported in $\geq 1\%$ of Patients		
	Alendronate once weekly 70 mg % (n=519)	Alendronate 10 mg/day % (n=370)
Gastrointestinal		
abdominal pain	3.7	3.0
dyspepsia	2.7	2.2
acid regurgitation	1.9	2.4
nausea	1.9	2.4
abdominal distension	1.0	1.4
constipation	0.8	1.6
flatulence	0.4	1.6
gastritis	0.2	1.1
gastric ulcer	0.0	1.1
Musculoskeletal		
musculoskeletal (bone, muscle or joint) pain	2.9	3.2
muscle cramp	0.2	1.1

Concomitant use with oestrogen/hormone replacement therapy

In two studies (of one and two years' duration) of postmenopausal osteoporotic women (total: n=853), the safety and tolerability profile of combined treatment with alendronate 10 mg once daily and oestrogen \pm progestin (n=354) was consistent with those of the individual treatments.

Men

In two, placebo-controlled, double blind, multicentre studies in men (a two year study of alendronate 10 mg/day (n = 146) and a one year study of alendronate once weekly 70 mg (n = 109), the safety profile of alendronate was generally similar to that seen in post menopausal women. The rates of discontinuation of therapy due to any clinical adverse experience were 2.7% for alendronate 10 mg/day vs. 10.5% for placebo, and 6.4% for alendronate once weekly 70 mg vs. 8.6% for placebo.

Other studies in Men and Women

In a ten week endoscope study in men and women (n=277; mean age: 55) no difference was seen in upper gastrointestinal tract lesions between alendronate once weekly 70 mg and placebo.

In an additional one-year study in men and women (n=335; mean age: 50) the overall safety and tolerability profiles of alendronate once weekly 70 mg were similar to that of placebo and no difference was seen between men and women.

Prevention of Osteoporosis in Postmenopausal Women

The safety of alendronate in postmenopausal women 40-60 years of age has been evaluated in three double-blind, placebo-controlled studies involving over 1,400 patients randomised to receive alendronate for either two or three years. In these studies, the safety and tolerability profile of alendronate 5 mg/day (n=642) was similar to that of placebo (n=648). The only adverse experience reported by the investigators as possibly, probably or definitely medicine related in $\geq 1\%$ of patients treated with alendronate 5 mg/day and at a greater incidence than placebo was dyspepsia (alendronate, 1.9% vs. placebo, 1.7%).

Concomitant use with Oestrogen/hormone replacement therapy

In two studies (of one and two years duration) of postmenopausal osteoporotic women (total: n=853), the safety and tolerability profile of combined treatment with alendronate 10 mg once daily and oestrogen \pm progestin (n=354) was consistent with those of the individual treatments.

Treatment and Prevention of Glucocorticoid-Induced Osteoporosis

In two, one-year, placebo controlled, double-blind, multicentre studies in patients receiving glucocorticoid treatment, the overall safety and tolerability profiles of alendronate 5 and 10 mg /day were generally similar to that of placebo. The following gastrointestinal adverse experiences were reported by the investigators as possibly, probably, or definitely medicine related in $\geq 1\%$ of patients treated with either alendronate 5 or 10 mg/day and at a greater incidence than placebo: abdominal pain (alendronate 10 mg, 3.2%; alendronate 5 mg, 1.9%; placebo, 0.0%), acid regurgitation (2.5%, 1.9%, 1.3%), constipation (1.3%, 0.6%, 0.0%), melena (1.3%, 0.0%, 0.0%) and nausea (0.6%, 1.2%, 0.6%).

The overall safety and tolerability profile in the glucocorticoid-induced osteoporosis population that continued therapy for the second year of the studies was consistent with that observed in the first year.

Paget's Disease of Bone

In clinical studies (Paget's disease and osteoporosis), adverse experiences reported in patients taking alendronate 40 mg/day for 3-12 months were similar to those in postmenopausal women treated with alendronate 10 mg/day. However, there was an apparent increased incidence of upper gastrointestinal adverse experiences in patients taking alendronate 40 mg/day. Isolated cases of oesophagitis and gastritis resulted in discontinuation of treatment.

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Additionally, musculoskeletal (bone, muscle or joint) pain, which has been described in patients with Paget's disease treated with other bisphosphonates, was reported by the investigators as possibly, probably, or definitely medicine related in approximately 6% of patients treated with alendronate 40 mg/day versus approximately 1% of patients treated with placebo, but rarely resulted in discontinuation of therapy.

Post-Marketing Experience

The following adverse reactions have been reported in post-marketing use with alendronate:

Body as a Whole: hypersensitivity reactions including urticaria and rarely, angioedema. As with other bisphosphonates, transient symptoms as in an acute-phase response (myalgia, malaise, asthenia and rarely, fever) have been reported with alendronate, typically in association with initiation of treatment. Rarely, symptomatic hypocalcaemia has occurred, generally in association with predisposing conditions. Rarely, peripheral oedema.

Gastrointestinal: nausea, vomiting, oesophagitis, oesophageal erosions, oesophageal ulcers, rarely oesophageal stricture or perforation, and oropharyngeal ulceration and/or stomatitis; rarely gastric or duodenal ulcers, some severe and with complications (see **Warnings and Precautions**, and **Dosage and Administration**). Localised osteonecrosis of the jaw, generally associated with tooth extraction and/or local infection (including osteomyelitis), often with delayed healing has been reported rarely (see **Warnings and Precautions**).

Musculoskeletal: bone, joint, and/or muscle pain, rarely severe and/or incapacitating (see **Warnings and Precautions**); joint swelling; low-energy femoral shaft fracture (see **Warnings and Precautions**).

Nervous System: dizziness, vertigo, dysgeusia.

Skin: rash (occasionally with photosensitivity), pruritus, alopecia, rarely severe skin reactions, including Stevens-Johnson syndrome and toxic epidermal necrolysis.

Special Senses: rarely uveitis, scleritis or episcleritis

INTERACTIONS

If taken at the same time it is likely that calcium supplements, antacids, and other oral medications will interfere with absorption of alendronate. Therefore, patients must wait at least one half hour after taking alendronate before taking any other oral medication.

No other medicine interactions of clinical significance are anticipated though the concomitant medication with two or more bisphosphonates cannot be recommended because of the lack of clinical data.

Concomitant use of HRT (oestrogen ± progestin) and alendronate was assessed in two clinical studies of one or two years' duration in postmenopausal osteoporotic women.

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Combined use of alendronate and HRT resulted in greater increases in bone mass, together with greater decreases in bone turnover, than seen with either treatment alone. In these studies, the safety and tolerability profile of the combination was consistent with those of the individual treatments (see **Adverse Effects**, Clinical Studies, Concomitant use with oestrogen/hormone replacement therapy).

Specific interaction studies were not performed. Alendronate was used in studies of treatment and prevention of osteoporosis in men, postmenopausal women and glucocorticoid users, with a wide range of commonly prescribed medicines without evidence of clinical adverse interactions. In clinical studies, the incidence of upper gastrointestinal adverse events was increased in patients receiving daily therapy with dosages of alendronate greater than 10 mg and aspirin-containing products. However, this was not observed in studies with alendronate tablet once weekly 70 mg.

Since NSAID use is associated with gastrointestinal irritation, caution should be used during concomitant use with alendronate.

OVERDOSAGE

No specific information is available on the treatment of overdose with alendronate. Hypocalcaemia, hypophosphataemia and upper gastrointestinal adverse events, such as upset stomach, heartburn, oesophagitis, gastritis, or ulcer, may result from oral overdose. Milk or antacids should be given to bind alendronate. Due to the risk of oesophageal irritation, vomiting should not be induced and the patient should remain fully upright.

Contact the Poisons Information Centre for advice regarding management of overdose.

PHARMACEUTICAL PRECAUTIONS

Instructions for Use/Handling

Store below 25°C.

Shelf life

24 months

MEDICINE CLASSIFICATION

Prescription Medicine.

PACKAGE QUANTITIES

AURO-ALENDRONATE alendronate (as sodium alendronate) 70 mg tablet is presented in pack size of 4 tablets in blister.

FURTHER INFORMATION

The chemical name of Alendronate sodium is:

(4-amino-1-hydroxybutylidene)-bisphosphonic acid monosodium salt, trihydrate

Alendronate sodium is a white or almost white, crystalline powder. It is sparingly soluble in water, practically insoluble in methanol and methylene chloride and has a molecular weight of 325.1.

Excipients

AURO-ALENDRONATE contains the following inactive ingredients: Cellulose - microcrystalline (Avicel PH-101 & PH-102), starch-maize, sodium starch glycollate type A, Povidone and magnesium stearate.

NAME AND ADDRESS

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DATE OF PREPARATION

05th July 2011