**PACKAGE INSERT TEMPLATE FOR ALENDRONATE TABLET**

**Brand or Product Name**
*[Product name]* Tablet 70mg
*[Product name]* Tablet 10mg

**Name and Strength of Active Substance(s)**

Alendronate sodium …mg equivalent to alendronate….mg

**Product Description**
*[Visual description of the appearance of the product (eg colour, markings etc)*
*eg White, circular flat beveled edge film-coated tablets marked '10' on one side*

**Pharmacodynamics**
Alendronate sodium is a bisphosphonate that binds to bone hydroxyapatite and inhibits osteoclast-mediated bone resorption. At the cellular level, it shows localization to sites of bone resorption and inhibits osteoclast resorption and activity. Alendronate sodium does not interfere with osteoclast recruitment to attachment

**Pharmacokinetics**
*Absorption*

- Like other bisphosphonates, alendronate is poorly absorbed after oral doses.
- Bioavailability: 0.7% (women), 0.59% (men)
- Absorption is decreased by food, especially by products containing calcium or other polyvalent cations

*Distribution*

- Volume of distribution is 2576 L
- Protein binding is approximately 78%

*Metabolism*

- Bisphosphonates do not appear to be metabolised.

*Elimination*

- About half of the absorbed portion is excreted in the urine; the remainder is sequestered to bone for a prolonged period
- Renal clearance is significantly reduced in patients with renal impairment

- Fecal excretion: minimal
- Elimination Half Life is 1.9 h

**Indication**

Alendronate is indicated for the treatment and prevention of osteoporosis in postmenopausal women.

- For the treatment of osteoporosis, alendronate increases bone mass and prevent fractures, including those of the hip and spine (vertebral compression fractures). Osteoporosis may be confirmed by the finding of low bone mass or by the presence or history of osteoporotic fracture.

- For the prevention of osteoporosis, alendronate 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; 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 alendronate for prevention of osteoporosis.

Alendronate is indicated for the treatment of osteoporosis in men to prevent fractures.

Alendronate is indicated for the treatment and prevention of glucocorticoid-induced osteoporosis in men and women.

**Recommended Dosage**

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.

To facilitate delivery to the stomach and thus reduce the potential for esophageal irritation, 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.

Alendronate should not be taken at bedtime or before arising for the day. Failure to follow these instructions may increase the risk of esophageal adverse experiences .

Patients should receive supplemental calcium and vitamin D, if dietary intake is inadequate .

No dosage adjustment is necessary for the elderly or for patients with mild-to-moderate renal insufficiency (creatinine clearance 35 to 60 mL/min. 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 70mg tablet once weekly
  Or
- One 10mg tablet once daily.

*Prevention of osteoporosis in postmenopausal women*

The recommended dosage is one 5 mg tablet once daily.

*Treatment and prevention of glucocorticoid-induced osteoporosis in men and women*

The recommended dose is 5mg once a day, except for postmenopausal women not receiving estrogen, for whom the recommended dosage is 10mg once a day.

Alendronate is not indicated for use in children.

**Mode of Administration**
Oral

*Updated November 2012*

## Contraindications

- esophageal abnormalities (eg, stricture or achalasia) which delay esophageal emptying
- hypersensitivity to alendronate or any component of the product
- hypocalcemia; resolve hypocalcemia prior to beginning therapy
- inability to stand or sit upright for 30 minutes

## Warnings and Precautions

- Alendronate should not be given to patients with abnormalities of the oesophagus or other factors that might delay oesophageal emptying, or those unable to stand or sit upright for at least 30 minutes. It should be used with caution in patients with upper gastrointestinal abnormalities.

To minimise the risk of oesophageal reactions:

- patients should be instructed to swallow alendronate tablets whole with plenty of water (not less than 200 mL), in an upright position (standing or sitting). Mineral water with a high concentration of calcium should be avoided
- tablets should be taken on rising for the day, on an empty stomach, at least 30 minutes before breakfast(or first food of the day) and any other oral medication
- patients should remain upright after taking the tablets (standing or sitting upright for at least 30 minutes), and should not lie down before eating the first meal of the day
- alendronate should not be taken at bedtime, or before getting up for the day

- active upper gastrointestinal disease (eg, dysphagia, esophageal diseases, duodenitis, gastritis, ulcers); may exacerbate condition
- atypical fractures of the thigh (subtrochanteric and diaphyseal femur fractures) have been reported in patients taking bisphosphonates for osteoporosis; therapy interruption in patients who develop evidence of a femoral shaft fracture may be necessary
- cancer diagnosis; increased risk of osteonecrosis of the jaw
- comorbid Barrett's esophagus; avoid use due to risk of esophageal cancer
- comorbid disorders (eg, periodontal and/or other preexisting dental disease, anemia, coagulopathy, infection, ill-fitting dentures); increased risk of osteonecrosis of the jaw
- concurrent therapies (eg, corticosteroids or chemotherapy); increased risk for osteonecrosis, especially in the jaw
- dental procedures, invasive (ie, tooth extraction, dental implants, boney surgery); increased risk of osteonecrosis of the jaw; discontinuing therapy may reduce risk

*Updated November 2012*

- esophageal adverse events, including bleeding and esophageal stricture or perforation, have been reported; discontinue if symptoms develop
- mental disabilities; preventing understanding of proper administration may lead to increased risk of severe esophageal adverse events
- musculoskeletal pain, severe; has been reported within days, months, or years following therapy initiation; consider discontinuing bisphosphonates if symptoms occur
- osteonecrosis of the jaw, generally associated with tooth extraction and/or local infection with delayed healing, has been reported
- poor oral hygiene; increased risk of osteonecrosis of the jaw
- renal insufficiency (creatinine clearance less than 35 mL/min); use not recommended
- ulcers, gastric and duodenal, some severe and with complications, have been reported
- Hypocalcaemia should be corrected before starting alendronate therapy, and other disorders affecting mineral metabolism such as vitamin D deficiency or hypoparathyroidism should also be treated; serum calcium in these patients should be monitored during therapy

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

- Patients should be instructed that if they miss a dose of 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.

- Due to the positive effects of alendronate in increasing bone mineral, small, asymptomatic decreases in serum calcium and phosphate may occur, especially in patients receiving glucocorticoids, in whom calcium absorption may be decreased. Ensuring adequate calcium and vitamin D intake is especially important in patients receiving glucocorticoids.

*Effects on the ability to drive and use machines*
No studies on the effects on the ability to drive and use machines has 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.

*Updated November 2012*

**Interactions with Other Medicaments**

The bisphosphonates are not well absorbed from the gastrointestinal tract, and dosage with food further impairs their absorption. Alendronate should not be administered with dairy products or meals. It is recommended that alendronate be administered two hours before a meal. The bioavailability of alendronate will also be diminished if it is administered one hour before a meal, during a meal, or two hours after a meal

There may be additive hypocalcaemic effects with aminoglycosides

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

Alendronate should not be administered concurrently with orange juice. It is recommended that alendronate be administered two hours before a meal. The bioavailability of alendronate will also be diminished if it is administered one hour before a meal, during a meal, or two hours after a meal.

If taken at the same time it is likely that calcium supplements, calcium, magnesium, or aluminum-containing 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.

**Statement on Usage During Pregnancy and Lactation**

*Pregnancy*

There is no data on fetal risk in humans. Animal data suggest that bisphosphonate uptake in fetal bone is greater than that into maternal bone; theoretically, fetal risk may exist after completing a course of treatment. Alendronate should be used in pregnant women only if the potential benefit justifies the potential risk to the mother and fetus

*Lactation*

It is not known whether alendronate is excreted into human breast milk, and the potential for adverse effects in the breastfeeding infant has not been determined. Use caution when administering alendronate to a nursing woman

*Updated November 2012*

**Adverse Effects / Undesirable Effects**
Neurologic: Headache, dizziness, vertigo, dysgeusia

Gastrointestinal: Abdominal pain ,Constipation ,Diarrhea , Flatulence , Indigestion , Vomiting , Duodenal ulcer disease, Esophageal erosions, Esophageal perforation, Esophageal stricture, Esophagitis ,Gastric ulcer ,Ulcerative pharyngitis, acute, Ulcer of esophagus

Immunologic: Hypersensitivity reaction

Musculoskeletal: Arthralgia, Aseptic necrosis of bone of jaw , Bone pain, Myalgia, joint swelling; low-energy femoral shaft fracture

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.

Other: Fever, Influenza-like symptoms, Disturbances in serum electrolytes may occur, most commonly hypocalcaemia and hypophosphataemia.. Other rare adverse effects include blood disorders such as anaemia, thrombocytopenia, leucopenia and disturbances in liver enzyme values.

**Overdose and Treatment**
*Symptoms*
No specific information is available on the treatment of overdosage with alendronate Overdosage with bisphosphonates would be likely to result in symptoms of hypocalcaemia, paresthesia, hypotension, fever, and vomiting and upper gastrointestinal adverse events, such as upset stomach, heartburn, esophagitis, gastritis, or ulcer, may result from oral overdosage.

*Treatment*
If necessary, parenteral infusion of a calcium salt could be given. Giving milk or antacids, to bind the bisphosphonate and minimize absorption, has been suggested for oral over dosage.

Due to the risk of esophageal irritation, vomiting should not be induced and the patient should remain fully upright.

Decontamination: Activated charcoal, gastric lavage

*Updated November 2012*

**Storage Conditions**
*[eg Store below….°C ]*

**Dosage Forms and Packaging Available**
*[Packaging type & pack size]*

**Name and Address of Manufacturer**
*[Name & full address of manufacturer]*

**Name and Address of Marketing Authorization Holder**
*[Name & full address of marketing authorization holder]*

**Date of Revision of Package Insert**
*[day/month/year ]*

*Updated November 2012*