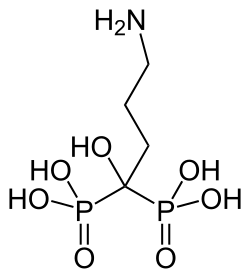
**NAME: ABDUL REHMAN**

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**DRUG MONOGRAPH**

**DRUG:  ALENDRONATE**

**INTRODUCTION:**  Synthetic bisphosphonate; bone resorption inhibitor.

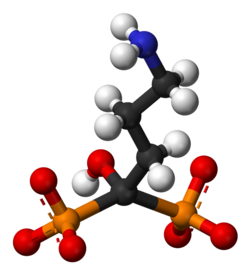
Alendronic acid was first described in 1978 and approved for medical use in the United States in 1995. It is available as a generic medication. In 2022, it was the 103rd most prescribed medication in the United States, with more than 6 million prescriptions.

**Drug class:**

* Bone Resorption Inhibitor
* Bisphosphonates

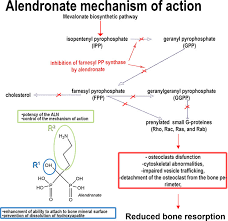
**Chemical name:** (4-Amino-1-hydroxybutylidene) bis-phosphonic acid,

Mono sodium salt, trihydrate.

**Molecular formula:** C4H13NO7P2•3H2O•Na

**MECHANISM OF ACTION:**

Nitrogen containing bisphosphonates, which include ibandronate, pamidronate and alendronate exert their effects on osteoclasts mainly by inhibiting the synthesis of isoprenoid lipids such as isopentenyl diphosphatee (IPP), farnesyl diphosphate (FPP), and geranylgeranyl diphosphate  via the mevalonate pathway. These isoprenoids are used in posttranslational modification (prenylation) of small GTPases such as Ras, Rho, and Rac. These prenylated GTPases are necessary for various cellular processes including osteoclast morphology, endosome trafficking, and apoptosis. Alendronate has also been shown to impair the function of osteclast lysosomes.

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**Brand names:** Fosamax, Binosto

**INDICATIONS AND DOSE**

**Treatment of postmenopausal osteoporosis**

* BY MOUTH
* Adult (female): 10 mg daily, alternatively 70 mg once weekly.

**Treatment of osteoporosis in men**

* BY MOUTH
* Adult (male): 10 mg daily.

**Prevention and treatment of corticosteroid-induced osteoporosis in postmenopausal women not receiving hormone replacement therapy**

* BY MOUTH
* Adult (female): 10 mg daily.

**OFF LABEL USE:**

* **Osteogenesis Imperfecta**

Used to increase bone density and reduce fracture risk in both children and adults with this genetic brittle-bone disorder.

* **Fibrous Dysplasia**

Employed to relieve bone pain and help stabilize lesions.

* **Complex Regional Pain Syndrome (CRPS)**

Bisphosphonates like alendronate are among the few medications with positive placebo-controlled evidence in CRPS.

* **Bone Metastases & Multiple Myeloma**

Though the specific FDA indication is for osteoporosis, alendronate is used off-label to reduce bone pain and fracture risk in cancers such as breast, lung, prostate metastases, and multiple myeloma.

* **Hypercalcemia of Malignancy**

While others like pamidronate/zoledronate are standard, alendronate has been used to lower elevated calcium due to cancer.

**KINETIC PROFILING:**

Bisphosphonate; binds to hydroxyapatite crystals in bone and inhibits osteoclast-mediated bone resorption; decreases mineral release and collagen or matrix breakdown in bone

**Absorption**

* Bioavailability (fasting): Women, 0.64%; men, 0.59%; reduced up to 60% by food
* Onset: 3 weeks
* Duration: 12-30 weeks (multiple doses)

**Distribution**

* Protein bound: 78%
* Vd 28 L (exclusive of bone)

**Metabolism**

* Not metabolized

**Elimination**

* Half-life: Up to 10 years in bone (terminal)
* Excretion: Urine 50%, feces (unabsorbed drug)

**DRUG INTERACTIONS:**

### Antacids or Mineral Supplements Containing Divalent Cations

Potential decreased alendronate absorption when administered with antacids, mineral supplements, or oral drugs containing multivalent cations (e.g., calcium).

### Other Oral Medications

Potential decreased alendronate absorption when administered concomitantly with other oral medications. Administer alendronate ≥30 minutes prior to other oral medications

|  |  |  |
| --- | --- | --- |
| Drug | Interaction | Comments |
| Antacids (calcium) | May interfere with absorption of alendronate | Wait ≥30 minutes after taking alendronate before taking any other oral medications |
| NSAIAs (e.g., aspirin) | Potential increased GI toxicity | Use caution |
| Prednisolone | No change In alendronate bioavailabilty |  |
| Ranitidine | IV ranitidine doubled alendronate bioavailability; however, clinical importance not known |  |

**Contraindications**

* Esophageal abnormalities that delay esophageal emptying (e.g., stricture, achalasia).
* Patients at increased risk of aspiration should not receive alendronate oral solution.
* Inability to stand or sit upright for at least 30 minutes.
* Hypocalcemia.
* Known hypersensitivity to alendronate or any ingredient in the formulation.

#### **Specific Populations**

##### **Pregnancy**

* Alendronate alone or in fixed combination with cholecalciferol: **Category C.**
* **Lactation**
* Not known whether alendronate is distributed into milk. Caution if used in nursing women.

##### **Pediatric Use**

* In randomized trial in pediatric patients (4–18 years of age) with osteogenesis imperfecta, treatment with alendronate did not reduce risk of fracture or bone pain; increased incidence of vomiting in children receiving alendronate compared with placebo. Manufacturer states that alendronate not indicated in children.

##### **Geriatric Use**

* No substantial differences in safety and efficacy relative to younger adults, but increased sensitivity cannot be ruled out.

##### **Hepatic Impairment**

* Not evaluated in patients with hepatic impairment.

**Renal Impairment** Use not recommended in patients with severe renal impairment (Clcr <35 mL/minute). (See Special Populations under Pharmacokinetics.)

**SIDE EFFECTS**

* **Common or very common** Gastrointestinal disorders-joint swelling vertigo
* Uncommon Haemorrhage
* **Rare or very rare** Femoral stress fracture oropharyngeal ulceration-photosensitivity reaction severe cutaneous adverse reactions (SCARS)
* **SIDE-EFFECTS, FURTHER** **INFORMATION** Severe oesophageal reactions (oesophagitis, oesophageal ulcers, oesophageal stricture and oesophageal erosions) have been reported; patients should be advised to stop taking the tablets and to seek medical attention if they develop symptoms of oesophageal irritation such as dysphagia, new or worsening heartburn, pain on swallowing or retrosternal’

**CAUTIONS !**

**Active gastro-intestinal bleeding. atypical femoral fractures. duodenitis dysphagia. exclude other causes of osteoporosis. gastritis history (within 1 year) of ulcers surgery of the upper gastro-intestinal tract symptomatic oesophageal disease ulcers upper gastro-intestinal disorders.**

**PATIENT AND CARER ADVICE**

Patients or their carers should be given advice on how to administer alendronic acid tablets and oral solution.Oesophageal reactions Patients (or their carers) should be advised to stop taking alendronic acid and to seek medical attention if they develop symptoms of oesophageal imitation such as dysphagia, new or worsening heartburn, pain on swallowing or retrosternal pain.

**References**

1. BNF 2024-25,Page;771
2. <https://en.wikipedia.org/wiki/Alendronic_acid>
3. <https://reference.medscape.com/drug/fosamax-binosto-alendronate-342810>