# OSTO-D Tablets

# اوسٹو۔ڈی گولیاں

**(Alendronate Sodium USP and Colecalciferol BP)**

(ایلنڈرونیٹ سوڈیم یو ایس پی اور کولی کیلسیفرول بی پی)

**COMPOSITION:** Each tablet contains: Alendronate Sodium USP eq. to Alendronic Acid 70mg. Colecalciferol BP 2800 IU
[BP Specs.]

**DESCRIPTION: Osto-D** tablet contains Colecalciferol (Vitamin $D_3$) which is produced in the skin by conversion of 7-dehydrocholesterol to Vitamin $D_3$ by ultraviolet light and Alendronate sodium which is a bisphosphonate that inhibits osteoclastic bone resorption.

**CLINICAL PHARMACOLOGY:**
**Mechanism of Action: Alendronate Sodium:** Alendronate sodium is a bisphosphonate that inhibits osteoclastic bone resorption with no direct effect on bone formation. Preclinical studies have shown preferential localisation of alendronate to sites of active resorption. Activity of osteoclasts is inhibited, but recruitment or attachment of osteoclasts is not affected. The bone formed during treatment with alendronate is of normal quality.
**Colecalciferol (Vitamin $D_3$):** In the absence of adequate sunlight exposure, Vitamin $D_3$ is an essential dietary nutrient. Vitamin $D_3$ is converted to 25-hydroxyvitamin $D_3$ in the liver, and stored until needed. Conversion to the active calcium-mobilizing hormone 1,25-dihydroxyvitamin $D_3$ (calcitriol) in the kidney is tightly regulated. The principal action of 1,25-dihydroxy vitamin $D_3$ is to increase intestinal absorption of both calcium and phosphate as well as regulate serum calcium, renal calcium and phosphate excretion, bone formation and bone resorption.

**PHARMACOKINETICS:**
**Alendronate Sodium: Absorption:** Relative to an intravenous reference dose, the oral mean bioavailability of alendronate in women was 0.64% for doses ranging from 5 to 70mg when administered after an over night fast and two hours before a standardised breakfast. Bioavailability was decreased similarly to an estimated 0.46% and 0.39% when alendronate was administered one hour or half an hour before a standardised breakfast.
**Distribution:** The mean steady-state volume of distribution, exclusive of bone, is at least 28 litres in humans. Concentrations of alendronate in plasma following therapeutic oral doses are too low for analytical detection (< 5ng/ml). Protein binding in human plasma is approximately 78%.
**Metabolism:** There is no evidence that alendronate is metabolised in animals or humans.
**Elimination:** Following a single intravenous dose of [$C^{14}$] 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 10mg intravenous dose, the renal clearance of alendronate was 71ml/min, and systemic clearance did not exceed 200ml/min. Plasma concentrations fell by more than 95% within six hours following intravenous administration.
**Colecalciferol: Absorption:** In healthy adult subjects (males and females), following administration of Alendronate/Colecalciferol after an overnight fast and two hours before a meal, the mean area under the serum-concentration-time curve (AUC0-120 hrs) for vitamin $D_3$ (unadjusted for endogenous vitamin $D_3$ levels) was 296.4ng·hr/ml.
**Distribution:** Following absorption, vitamin $D_3$ enters the blood as part of chylomicrons. Vitamin $D_3$ is rapidly distributed mostly to the liver where it undergoes metabolism to 25-hydroxy vitamin $D_3$, the major storage form. Lesser amounts are distributed to adipose and muscle tissue and stored as vitamin $D_3$ at these sites for later release into the circulation. Circulating vitamin $D_3$ is bound to vitamin D-binding protein.
**Metabolism:** Vitamin $D_3$ is rapidly metabolized by hydroxylation in the liver to 25-hydroxy vitamin $D_3$, and subsequently metabolized in the kidney to 1,25-dihydroxyvitamin $D_3$, which represents the biologically active form. Further hydroxylation occurs prior to elimination. A small percentage of vitamin $D_3$ undergoes glucuronidation prior to elimination.
**Elimination:** When radioactive Vitamin $D_3$ was administered to healthy subjects, the mean urinary excretion of radioactivity after 48 hours was 2.4%, and the mean faecal excretion of radioactivity after 4 days was 4.9%. In both cases, the excreted radioactivity was almost exclusively as metabolites of the parent.

**INDICATIONS:** Alendronic Acid/Colecalciferol is indicated for the treatment of postmenopausal osteoporosis in women at risk of vitamin D insufficiency. Alendronic Acid/Colecalciferol reduces the risk of vertebral and hip fractures.

**DOSAGE AND ADMINISTRATION:**
**Recommended Dosing:** The recommended dose is one Alendronic Acid/Colecalciferol tablet once weekly. Patients should receive supplemental calcium if intake from diet is inadequate. Additional supplementation with vitamin D should be considered on an individual basis taking into account any Vitamin D intake from vitamins and dietary supplements.
**Patients with renal impairment:** Alendronic Acid/Colecalciferol is not recommended for patients with renal impairment where creatinine clearance is less than 35ml/min, due to lack of experience. No dose adjustment is necessary for patients with a creatinine clearance greater than 35ml/min.
**Elderly:** In clinical studies there was no age-related difference in the efficacy or safety profiles of alendronate. Therefore no dose adjustment is necessary for the elderly.

**PAEDIATRIC POPULATION:** The safety and efficacy of Alendronic Acid/Colecalciferol in children less than 18 years of age have not been established. Alendronic Acid/Colecalciferol should not be used in children less than 18 years of age.

**CONTRAINDICATIONS:**
- Abnormalities of the oesophagus and other factors which delay oesophageal emptying such as stricture or achalasia.
- Inability to stand or sit upright for at least 30 minutes.
- Hypocalcaemia

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**WARNINGS AND PRECAUTIONS:**
**Alendronate: Upper gastrointestinal adverse reactions:** Alendronate can cause local irritation of the upper gastrointestinal mucosa.
**Osteonecrosis of the jaw:** Osteonecrosis of the jaw, generally associated with tooth extraction and/or local infection (including osteomyelitis), has been reported in patients with cancer who are receiving treatment regimens including primarily intravenously administered bisphosphonates.
**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. The time to onset of symptoms varied from one day to several months after starting treatment.
**Atypical fractures of the femur:** Atypical subtrochanteric and diaphyseal femoral fractures have been reported with bisphosphonate therapy, primarily in patients receiving long-term treatment for osteoporosis.
**Renal impairment:** Alendronic Acid/Colecalciferol is not recommended for patients with renal impairment where creatinine clearance is less than 35ml/min.
**Bone and mineral metabolism:** Hypocalcaemia must be corrected before initiating therapy with Alendronic Acid/Colecalciferol
**Colecalciferol:** Vitamin $D_3$ may increase the magnitude of hypercalcaemia and/or hypercalciuria when administered to patients with disease associated with unregulated overproduction of calcitriol (e.g. leukaemia, lymphoma, sarcoidosis). Urine and serum calcium should be monitored in these patients. Patients with malabsorption may not adequately absorb vitamin $D_3$.
**Pregnancy and Lactation:** Alendronate/Colecalciferol is only intended for use in postmenopausal women and therefore it should not be used during pregnancy or in breast-feeding women.

**PREGNANCY:** There are no or limited amount of data from the use of Alendronate in pregnant women. Alendronic Acid/Colecalciferol should not be used during pregnancy.
**Breast-feeding:** It is unknown whether Alendronate/Colecalciferol metabolites are excreted in human milk. A risk to the newborns/infants cannot be excluded. Alendronate should not be used during breast-feeding.

**SIDE EFFECTS:**

| System Organ Class | Frequency | Adverse Reactions |
|---|---|---|
| **Nervous system disorders:** | Common | headache, dizziness† |
| | Uncommon | dysgeusia† |
| **Gastrointestinal disorders:** | Common | abdominal pain, dyspepsia, constipation, diarrhoea, flatulence, oesophageal ulcer*, dysphagia*, abdominal distension, acid regurgitation. |
| | Uncommon | nausea, vomiting, gastritis, oesophagitis*, oesophageal erosions*, melena† |
| **Skin and subcutaneous tissue disorders:** | Common | alopecia†, pruritus† |
| | Uncommon | rash, erythema |
| **General disorders and administration site conditions:** | Common | asthenia†, peripheral oedema† |
| | Uncommon | transient symptoms as in an acute-phase response (myalgia, malaise and rarely, fever), typically in association with initiation of treatment† |

**DRUG INTERACTIONS: Interactions with other medicinal products: Alendronate:** If taken at the same time, it is likely that food and beverages (including mineral water), calcium supplements, antacids, and some oral medicinal products will interfere with absorption of alendronate. Therefore, patients must wait at least 30 minutes after taking alendronate before taking any other oral medicinal product.
**Colecalciferol:** Olestra, mineral oils, orlistat, and bile acid sequestrants (e.g. cholestyramine, colestipol) may impair the absorption of Vitamin D. Anticonvulsants, cimetidine and thiazides may increase the catabolism of Vitamin D. Additional vitamin D supplements may be considered on an individual basis.

**OVERDOSE: Alendronate: Symptoms:** Hypocalcaemia, hypophosphataemia and upper gastrointestinal adverse reactions, such as upset stomach, heartburn, oesophagitis, gastritis, or ulcer, may result from oral overdose.
**Management:** In case of overdose with Alendronic Acid/Colecalciferol, milk or antacids should be given to bind alendronate. Owing to the risk of oesophageal irritation, vomiting should not be induced and the patient should remain fully upright.
**Colecalciferol:** Vitamin D toxicity has not been documented during chronic therapy in generally healthy adults at a dose less than 10,000IU/day. In a clinical study of healthy adults a 4,000IU daily dose of Vitamin D3 for up to five months was not associated with hypercalciuria or hypercalcaemia.

**INSTRUCTIONS:** Store below 30°C. Protect from heat, light and moisture. Keep out of the reach of children.

**PRESENTATION: Osto-D tablets** (Alendronic Acid 70mg and Colecalciferol 2800IU) are available in a blister pack of 4's.

**ہدایات:** ۳۰ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔ گرمی، روشنی اور نمی سے بچائیں۔ بچوں کی پہنچ سے دور رکھیں۔

PHARMA
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