Strondex®

Alendronate Sodium

FORMS AND PRESENTATION
Strondex® 5: Tablets: Box of 30.
Strondex®10: Tablets: Box of 30.
Strondex® 35: Tablets: Box of 4.
Strondex® 70: Tablets: Box of 4.

COMPOSITION
Strondex® 5: Each tablet contains Alendronate Sodium equivalent to Alendronic Acid 5mg.
Strondex® 10: Each tablet contains Alendronate Sodium equivalent to Alendronic Acid 10mg.
Strondex® 35: Each tablet contains Alendronate Sodium equivalent to Alendronic Acid 35mg.
Strondex® 70: Each tablet contains Alendronate Sodium equivalent to Alendronic Acid 70mg.
Excipients: lactose, microcrystalline cellulose, magnesium stearate.

PHARMACOLOGICAL PROPERTIES
Pharmacodynamic properties
Therapeutic class: Drugs for treatment of bone diseases.
ATC code: M05BA04.
Alendronate Sodium is a bisphosphonate that inhibits osteoclastic bone resorption with no direct effect on bone formation. Preclinical studies have shown preferential localisation of Alendronic Acid 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 alendronic acid is of normal quality.
Pharmacokinetic properties
Absorption
Relative to an intravenous (IV) reference dose, the oral bioavailability of Alendronate in women was 0.7% for doses ranging from 5 to 40 mg when administered after an overnight fast and two hours before a standardized breakfast. Oral bioavailability in men (0.6%) was similar to that in women. Bioavailability was decreased similarly to an estimated 0.46% and 0.39% when Alendronate was administered one hour or half an hour before a standardized breakfast. In osteoporosis studies, Alendronate Sodium was effective when administered at least 30 minutes before the first food or beverage of the day.
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%.
In healthy subjects, oral prednisone (20 mg three times daily for five days) did not produce a clinically meaningful change in oral bioavailability of Alendronate (a mean increase ranging from 20% to 44%).
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 liters in humans. Concentrations of drug in plasma following therapeutic oral doses are too low for analytical detection (<5 ng/ml). Protein binding in human plasma is approximately 78%.
Biotransformation
There is no evidence that Alendronate is metabolized 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 feces. 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 six hours following IV administration. The terminal half-life in humans is estimated to exceed ten years, reflecting release of Alendronate from the skeleton. Alendronate is not excreted through the acidic or basic transport systems of the kidney in rats, and thus it is not anticipated to interfere with the excretion of other drugs by those systems in humans.

INDICATIONS
Strondex® is indicated for:
- The treatment of osteoporosis in post-menopausal women to prevent fractures.
- The treatment of osteoporosis in men to prevent fractures.
- The treatment of glucocorticoid-induced osteoporosis and prevention of bone loss in post-menopausal women considered at risk of developing the disease.

Risk factors often associated with the development of osteoporosis include thin body build, family history of osteoporosis, early menopause, moderately low bone mass and long-term glucocorticoid therapy, especially with high doses (≥15 mg/day).

CONTRAINDICATIONS
Alendronic Acid is contraindicated in:
- Abnormalities of the esophagus and other factors which delay esophageal emptying such as stricture or achalasia.
- Inability to stand or sit upright for at least 30 minutes.
- Hypersensitivity to Alendronic Acid or to any of the excipient.
- Hypocalcemia.

PRECAUTIONS
- Alendronic Acid can cause local irritation of the upper gastro-intestinal mucosa. Because there is a potential for worsening of the underlying disease, caution should be used when Alendronic Acid tablet is given to patients with active upper gastro-intestinal problems, such as dysphagia, esophageal disease, gastritis, duodenitis, ulcers or with a recent history (within the previous year) of major gastro-intestinal disease such as peptic ulcer, or active gastro-intestinal bleeding, or surgery of the upper gastro-intestinal tract other than pyloroplasty. In patients with known Barrett's esophagus, prescribers should consider the benefits and potential risks of Alendronate on an individual patient basis.
- Esophageal reactions (sometimes severe and requiring hospitalization), such as esophagitis, esophageal ulcers and esophageal erosions, rarely followed by esophageal stricture or perforation, have been reported in patients receiving Alendronic Acid. Physicians should therefore be alert to any signs or symptoms signaling a possible esophageal reaction and patients should be instructed to discontinue Alendronic Acid tablet and seek medical attention if they develop symptoms of esophageal irritation such as dysphagia, pain on swallowing or retrosternal pain, new or worsening heartburn.
- The risk of severe esophageal adverse experiences appears to be greater in patients who fail to take Alendronic Acid properly and/or who continue to take Alendronic Acid tablet after developing symptoms suggestive of esophageal irritation. It is very important that the full dosing instructions are provided to, and understood by the patient. Patients should be informed that failure to follow these instructions may increase their risk of esophageal problems.
- 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.
- Osteonecrosis of the jaw, generally associated with tooth extraction and/or local infection (including osteomyelitis), has been reported in patients with cancer receiving treatment regimens including primarily intravenously administered bisphosphonates. Many of these patients were also receiving chemotherapy and corticosteroids. Osteonecrosis of the jaw has also been reported in patients with osteoporosis receiving oral bisphosphonates.
- A dental examination with appropriate preventive dentistry should be considered prior to treatment with bisphosphonates in patients with concomitant risk factors (e.g. cancer, chemotherapy, radiotherapy, corticosteroids, poor oral hygiene, periodontal disease). While on treatment, these patients should avoid invasive dental procedures if possible. For patients who develop osteonecrosis of the jaw while on bisphosphonate therapy, 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 of osteonecrosis of the jaw. Clinical judgment of the treating physician should guide the management plan of each patient based on individual benefit/risk assessment.
- During bisphosphonate treatment, all patients should be encouraged to maintain good oral hygiene, receive routine dental check-ups, and report any oral symptoms such as dental mobility, pain or swelling.
- 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. Most patients had relief of symptoms after stopping. A subset had recurrence of symptoms when rechallenged with the same drug or another bisphosphonate.
- Stress fractures (also known as insufficiency fractures) of the proximal femoral shaft have been reported in patients treated long-term with Alendronic Acid (time to onset in the majority of cases ranged from 18 months to 10 years). The fractures occurred after minimal or no trauma and some patients experienced thigh pain, often associated with imaging features of stress fractures, weeks to months before presenting with a completed femoral fracture. Fractures were often bilateral; therefore the contralateral femur should be examined in bisphosphonate-treated patients who have sustained a femoral shaft fracture. Poor healing of these fractures was also reported. Discontinuation of bisphosphonate therapy in patients with stress fracture is advisable pending evaluation of the patient, based on an individual benefit risk assessment. During bisphosphonate treatment patients should be advised to report any thigh, hip or groin pain and any patient presenting with such symptoms should be evaluated for an incomplete femur fracture.
- Patients should be instructed that if they miss a dose of Alendronic Acid once weekly tablet, 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.
- Alendronic Acid tablet is not recommended for patients with renal impairment where GFR is less than 35 ml/min. Causes of osteoporosis other than estrogen deficiency, ageing and glucocorticoid use should be considered.
- Hypocalcemia must be corrected before initiating therapy with Alendronic Acid. Other disorders affecting mineral metabolism (such as vitamin D deficiency and hypoparathyroidism) should also be effectively treated. In patients with these conditions, serum calcium and symptoms of hypocalcemia should be monitored during therapy with Alendronic Acid.
- Due to the positive effects of Alendronic Acid in increasing bone mineral, decreases in serum calcium and phosphate may occur especially in patients taking glucocorticoids in which calcium absorption may be decreased. These are usually small and asymptomatic. However, there have been rare reports of symptomatic hypocalcemia, which have occasionally been severe and often occurred in patients with predisposing conditions (e.g. hypoparathyroidism, vitamin D deficiency and calcium malabsorption).
- Ensuring adequate calcium and vitamin D intake is particularly important in patients receiving glucocorticoids.

- This medicinal product contains lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicinal product.

Ability to drive and use machines

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 Alendronic Acid may affect some patients' ability to drive or operate machinery. Individual responses to Alendronic Acid may vary.

PREGNANCY AND LACTATION

There are no adequate data from the use of Alendronic Acid in pregnant women. Animal studies do not indicate direct harmful effects with respect to pregnancy, embryonal/fetal development, or postnatal development. Alendronic acid given during pregnancy in rats caused dystocia related to hypocalcemia. Given the indication, Alendronic Acid should not be used during pregnancy.

It is not known whether Alendronic Acid is excreted into human breast milk. Given the indication, Alendronic Acid tablet should not be used by breast-feeding women.

DRUG INTERACTIONS

- 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 Alendronic Acid. Therefore, patients must wait at least 30 minutes after taking Alendronic Acid before taking any other oral medicinal product.
- No other interactions with medicinal products of clinical significance are anticipated. A number of patients in the clinical trials received estrogen (intravaginal, transdermal, or oral) while taking Alendronic Acid. No adverse experiences attributable to their concomitant use were identified.
- Since NSAID use is associated with gastrointestinal irritation, caution should be used during concomitant use with Alendronate.
- Although specific interaction studies were not performed, in clinical studies Alendronic Acid was used concomitantly with a wide range of commonly prescribed medicinal products without evidence of clinical adverse interactions.

ADVERSE EFFECTS

The adverse experiences are listed below by body system, organ class and absolute frequency. They have been reported during clinical studies and/or post-marketing use.

Frequencies are defined as: Common (≥ 1/100 to <1/10), uncommon (≥ 1/1000 to <1/100), rare (≥ 1/10,000 to <1/1000), very rare (<1/10,000), not known (cannot be estimated from the available data).

- Immune system disorders: Hypersensitivity reactions including urticaria and angioedema (rare).
- Metabolism and nutrition disorders: symptomatic hypocalcaemia, often in association with predisposing conditions (rare).
- Nervous system disorders: Headache (common).
- Eye disorders: Uveitis, scleritis, episcleritis (rare).
- Gastrointestinal disorders: Abdominal pain, dyspepsia, constipation, diarrhea, flatulence, esophageal ulcer, dysphagia, abdominal distension, acid regurgitation (common); nausea, vomiting, gastritis, esophagitis, esophageal erosions, melena (uncommon); esophageal stricture, oropharyngeal ulceration, upper gastrointestinal PUBs (perforation, ulcers, bleeding) (rare).
- Skin and subcutaneous tissue disorders: Rash, pruritus, erythema (uncommon); rash with photosensitivity (rare); isolated cases of severe skin reactions including Stevens-Johnson syndrome and toxic epidermal necrolysis (very rare and isolated cases).
- Musculoskeletal, connective tissue and bone disorders: Musculoskeletal (bone, muscle or joint) pain (common); osteonecrosis of the jaw; severe musculoskeletal (bone, muscle or joint) pain; atypical subtrochanteric and diaphyseal femoral fractures (bisphosphonate class adverse reaction) (rare).
- General disorders and administration site conditions: Transient symptoms as in an acute-phase response (myalgia, malaise and rarely, fever), typically in association with initiation of treatment (rare).

During post-marketing experience the following reactions have been reported (frequency unknown):

- Nervous system disorders - rare: Dizziness, dysgeusia.
- Ear and labyrinth disorders: Vertigo.
- Skin and subcutaneous tissue disorders: Alopecia.
- Musculoskeletal, connective tissue and bone disorders: Joint swelling, stress fractures of the proximal femoral shaft.
- General disorders and administration site conditions: Asthenia, peripheral edema.

Laboratory test findings: In clinical studies, asymptomatic, mild and transient decreases in serum calcium and phosphate were observed in approximately 18 and 10%, respectively, of patients taking Alendronic Acid tablet 10 mg/day versus approximately 12 and 3% of those taking placebo. However, the incidences of decreases in serum calcium to <8.0 mg/dl (2.0 mmol/l) and serum phosphate to ≤ 2.0 mg/dl (0.65 mmol/l) were similar in both treatment groups.

DOSAGE AND ADMINISTRATION

The optimal duration of bisphosphonate treatment for osteoporosis has not been established. The need for continued treatment should be re-evaluated periodically based on the benefits and potential risks of Strondex® on an individual patient basis, particularly after 5 or more years of use.

Treatment of Osteoporosis in Postmenopausal Women

The recommended dosage is: One 70 mg tablet once weekly or one 10 mg tablet once daily.

Prevention of Osteoporosis in Postmenopausal Women

The recommended dosage is: One 35 mg tablet once weekly or one 5 mg tablet once daily.

Treatment to Increase Bone Mass in Men with Osteoporosis

The recommended dosage is: One 70 mg tablet once weekly or one 10 mg tablet once daily.

Treatment of Glucocorticoid-Induced Osteoporosis

The recommended dosage is one 5 mg tablet once daily, except for postmenopausal women not receiving estrogen, for whom the recommended dosage is one 10 mg tablet once daily.

Strondex® tablet must be taken at least 30 minutes before the first food, beverage, or medicinal product of the day with plain water only. Other beverages (including mineral water), food and some medicinal products are likely to reduce the absorption of Strondex®.

To facilitate delivery to the stomach and thus reduce the potential for local and esophageal irritation/adverse experiences:

- Strondex® tablet should only be swallowed upon arising for the day with a full glass of water (not less than 200 ml).
- Patients should not chew the tablet or allow the tablet to dissolve in their mouths because of a potential for oropharyngeal ulceration.
- Patients should not lie down until after their first food of the day which should be at least 30 minutes after taking the tablet.
- Patients should not lie down for at least 30 minutes after taking Strondex® tablet.
- Strondex® tablet should not be taken at bedtime or before arising for the day.

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

Use in the elderly

In clinical studies there was no age-related difference in the efficacy or safety profiles of Strondex®. Therefore no dosage adjustment is necessary for the elderly.

Use in renal impairment

No dosage adjustment is necessary for patients with GFR greater than 35 ml/min. Strondex® is not recommended for patients with renal impairment where GFR is less than 35 ml/min, due to lack of experience.

Pediatric patients

Strondex® is not recommended for use in children under the age of 18 years due to insufficient data on safety and efficacy in conditions associated with pediatric osteoporosis.

The use of Strondex® 70 has not been investigated in the treatment of glucocorticoid-induced osteoporosis.

OVERDOSAGE

Hypocalcemia, hypophosphatemia and upper gastro-intestinal adverse events, such as upset stomach, heartburn, esophagitis, gastritis, or ulcer, may result from oral overdosage.

No specific information is available on the treatment of overdosage with Alendronic Acid. Milk or antacids should be given to bind Alendronic Acid tablet. Owing to the risk of esophageal irritation, vomiting should not be induced and the patient should remain fully upright.

STORAGE CONDITIONS

Store below 30°C.

Keep in original pack in intact conditions.

Date of revision: September 2015.

This is a medicament

- A medicament is a product which affects your health, and its consumption contrary to instructions is dangerous for you
- Follow strictly the doctor's prescription, the method of use, and the instructions of the pharmacist who sold the medicament
- The doctor and the pharmacist are experts in medicine, its benefits and risks
- Do not by yourself interrupt the period of treatment prescribed for you
- Do not repeat the same prescription without consulting your doctor
- Medicament: keep out of reach of children

Council of Arab Health Ministers
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