APPROVED
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INSTRUCTION
for medical use
ALENDRA®

Composition:
active subspace: alendronic acid;
1 tablet contains sodium alendronate, equivalent to alendronic acid 70 mg;
excipients: microcrystalline cellulose, lactose monohydrate, croscarmellose sodium, magnesium stearate, colloidal anhydrous silica.

Pharmaceutical form. Tablets.

Pharmacotherapeutic group.
Drugs that influence on bone structure and mineralization. Code ATC M05B A04.

Clinical characteristics.
Indications.
Treatment of postmenopausal osteoporosis. The drug reduces risk of femoral and vertebral fractures.

Contraindications.
Hypersensitivity to sodium alendronate or to any other component of the drug; pathology of the esophagus (stricture or achalasia) that results in delayed evacuation of the contents of esophagus; inability to stand or sit upright for 30 minutes after taking the drug; hypocalcaemia; severe renal insufficiency (creatinine clearance <35 ml / min).

Dosage and administration.
Recommended dose: 1 tablet 70 mg 1 time per week.
The duration of treatment is determined by the physician.
The tablet should be taken with water at least 30 minutes before the first meal, drink or intake of other drugs. Other drinks (including mineral water), food and some drugs may reduce absorption of alendronate.
To facilitate penetration of the drug into the stomach and thus to reduce its irritating effect on the mucous tunic of the mouth, pharynx and esophagus, it is necessary to:
- take the drug with a glass of water (not less than 200 mL) in the morning after getting out of bed;
- avoid chewing the tablet, as this may cause ulcers of the mouth and pharynx;
- the first meal during the day should be taken only 30 minutes after taking the tablet;
- after taking the tablets the patients should not lie for at least 30 minutes;
- it is not recommended to take the drug before going to bed, or before getting out of bed after nocturnal sleep.

The interval between taking alendronate and other oral drugs should take at least one hour.
It is necessary to take calcium and vitamin D additionally if dietary intake is inadequate.
The drug should be taken on the same day of the week. If a dose is missed, it is necessary to take one tablet on the next day. In future the drug should be taken as usual; the next tablet should be used on the day chosen from the start of treatment.
Use in elderly patients:
No dosage adjustment is necessary in elderly patients.
Renal impairment:
No dosage adjustment is needed in patients with creatinine clearance greater than 35 mL/min. The effect of the drug during the treatment of osteoporosis caused by corticosteroids has not been studied.

Adverse reactions.
Nervous system disorders: headache; dizziness; vertigo; dysgeusia (bitter or unusual taste in the mouth after taking the drug).
Eye disorders: uveitis; scleritis; episcleritis.
Gastrointestinal disorders: abdominal pain; dyspepsia; constipation; diarrhoea; flatulence; ulcers of the mouth; pharynx and esophagus; dysphagia; abdominal distension; heartburn; regurgitation of gastric contents; nausea; vomiting; gastritis; esophagitis; esophageal erosion; esophageal stricture; perforation, ulcers, bleeding of the gastrointestinal tract (including oral cavity, pharynx, esophagus, stomach); melena.
Skin and subcutaneous tissue disorders: rash; urticaria; pruritus; erythema (redness); rash with photosensitivity; isolated cases of severe skin reactions, including Stevens-Johnson syndrome and toxic epidermal necrolysis; loss of hair (alopecia).
Musculoskeletal system disorders: bone, muscle or joint pain; osteonecrosis; femoral fractures, swelling of joints.
Metabolic disorders: symptomatic hypocalcaemia, often associated with the provoking factors.
General disorders: transient symptoms (muscle pain, malaise, fever) which are typically associated with the initiation of treatment; asthenia; peripheral swelling.
Immune system disorders: allergic reactions, including rash and angioneurotic edema.
Laboratory test findings: hypocalcaemia, hypophosphatemia (in treatment with alendronate 10 mg/kg per day).

Overdose.
Symptoms: hypocalcaemia, hypophosphatemia, indigestion, heartburn, esophagitis, gastritis or gastric ulcer.
Treatment: milk or antacids should be taken to bind alendronate. Owing to the risk of esophageal irritation, vomiting should not be induced and the patient should remain fully upright.

Using during pregnancy or breast-feeding.
The drug is not administered.

Children.
Do not use in children.

Precautions for use.
The drug can cause local irritation of the upper gastro-intestinal mucosa. Since there is a potential for exacerbation of the underlying disease, caution should be used when alendronate is given to patients with dysphagia, esophageal disease, gastritis, duodenitis, ulcers, as well as with a recent history (within the previous year) of major gastro-intestinal disease (peptic ulcer, active gastro-intestinal bleeding, surgery of the upper gastrointestinal 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.
As using the drug may cause esophagitis (inflammation of the esophagus), esophageal ulcers or esophageal erosions which may be rarely worsened by esophageal stricture, close monitoring for any manifestations of such influence is necessary. In case of such symptoms as dysphagia, pain on swallowing or retrosternal pain, heartburn (emergence or worsening of existing heartburn) stop the drug and seek medical attention.
A dental examination with appropriate preventive dentistry should be considered prior to treatment with bisphosphonates in patients with concomitant risk factors of osteonecrosis of the jaw (such as cancer, chemotherapy, radiotherapy, corticosteroids, inadequate oral hygiene, smoking, periodontal disease, osteoporosis). During the treatment such patients should avoid invasive dental interventions. Dental surgery may only exacerbate the condition of patients developing osteonecrosis of the jaw while on bisphosphonate therapy. There are no additional data or information available to suggest that withdrawal of bisphosphonates could reduce the risk of osteonecrosis of the jaw in patients who need dental interventions.

Before starting therapy with Alendra®, hypocalcaemia should be treated. Also, effective treatment of other mineral metabolism disorders (such as vitamin D deficiency and hypothyroidism/ hypothyroidism) is necessary. During the drug therapy, serum calcium level and symptoms of hypocalcaemia should be monitored in patients with such conditions.
Due to the possible effect of alendronate on increased bone mineralization, serum calcium and phosphate levels may decrease, especially in patients who take glucocorticoids, which may decrease calcium absorption. It is usually insignificant and asymptomatic. However, asymptomatic hypocalcaemia has been reported, it sometimes was severe and often occurred in patients with predisposing factors (such as hypothyroidism, vitamin D deficiency and malabsorption of calcium). Therefore, sufficient intake of calcium and vitamin D is especially important for patients taking glucocorticoids.
Due to the possible bilateral fractures of the proximal femur during chronic administration of the drug (more than 18 months) the contralateral femur should be examined in patients who have sustained a femoral shaft fracture. Also, due to the poor healing of such fractures, discontinuation of bisphosphonate therapy should be considered pending evaluation of the patient, based on an individual risk/benefit assessment.
This drug is not administered in patients with rare hereditary diseases, such as: galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption.

Ability to affect the reaction rate when driving motor transport or operating other mechanisms.
No effect on the ability to drive motor transport and use mechanisms has been observed. However, certain adverse reactions that have been reported with the drug, may affect some patients' ability to drive or operate machinery.

Drug interaction and other types of interactions.
If taken at the same time, it is likely that calcium drugs (including food supplements) and antacids will interfere with absorption of alendronate. The interval between taking alendronate and other oral drugs should take not less than one hour.
Co-administration of sodium alendronate and hormone replacement therapy (estrogen + progesterones) resulted in a greater increase of the bone mass and a significant reduction in bone resorption compared with sodium alendronate monotherapy.
Nonsteroidal anti-inflammatory drugs increase gastrointestinal effect of sodium alendronate.
Concomitant administration of sodium alendronate and glucocorticosteroids may increase hypocalcaemia, since glucocorticosteroids suppress the activity of vitamin D, which reduces the absorption of calcium and increases its excretion.
Caution should be used when prescribing alendronate with aminoglycosides, which decrease serum calcium level for a long time.
In the treatment of malignant hypercalcaemia, administration of thiazides, which reduce loss of calcium with the urine, may suppress the calcium-decreasing effect of sodium alendronate.
No other interactions with medicinal products of clinical significance are anticipated.

Pharmacological properties.
Pharmacodynamics. Sodium alendronate belongs to a group of aminobisphosphonates. It is a synthetic analogue of natural pyrophosphate. It inhibits precipitation of calcium phosphate, blocking its transformation into hydroxyapatite, delays aggregation of apatite crystals to form larger crystals and accelerates the resolution of these crystals. Its selective effect is due to high affinity of bisphosphonates and mineral components of the bone. It acts as effective non-hormonal specific inhibitor of osteoclast-mediated bone resorption. The exact mechanisms of this process are not fully clarified. It renews positive balance between bone resorption and formation. It increases bone mineral density of the spine, pelvis, etc., contributes to the formation of bone tissue with normal histological structure. It prevents new fractures. It reduces serum calcium level by inhibition of bone resorption and reduction of calcium release from the bone tissue. Calcium-reducing effect of the drug, mediated by inhibition of osteoclasts, is observed in 1 - 2 days.

Pharmacokinetics. Sodium alendronate is absorbed in gastrointestinal tract by 25%. The absolute bioavailability of tablets (5 to 10 mg), taken on empty stomach 2 hours before the meal is 0.64% (for women) and 0.59% (for men). Bioavailability is reduced (approximately by 40%) when taking alendronate half an hour – an hour before the usual breakfast. Bioavailability of alendronate is insignificant when using it with meal or within 2 hours after the meal. Taking alendronate simultaneously with other drinks (including mineral water, coffee, orange juice) decreases its bioavailability by 60%. Studies conducted on laboratory rats have shown that the intravenous dose of alendronate 1 mg/kg is temporarily distributed in soft tissues, but then it is rapidly redistributed. Half of the absorbed dose is excreted mainly by the kidneys unchanged within 72 hours, and the rest accumulates in bone tissue for a long time and is eliminated very slowly due to bonding with bone tissue. Half-life of alendronate in the bones is several years.
Alendronate is bound approximately 78% to plasma proteins and is not metabolized. Its plasma concentration is low (less than 5hg/mL) and it decreases by 95% within 6 hours after intravenous infusion.
After single oral administration of 10 mg alendronate, its renal clearance was 71 mL/min, and its systemic clearance did not exceed 200 mL/min.

Pharmaceutical characteristics:
general physico-chemical properties: white to off-white oval biconvex tablets.

Shelf-life. 3 years.

Storage conditions.
Store at the temperature not more than 25 °C in the original package.
Keep out of reach of children.

Package.
4 tablets are in a blister, each is in a carton envelope.

Conditions of supply.
On prescription.

Manufacturer.
KUSUM HEALTHCARE PVT. LTD.

Address.
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Date of last review.