Scheduling status **S3**

Proprietary name and dosage form:

Alendronate 70 Oethmaan tablets

Composition:

Each Alendronate 70 Oethmaan tablet contains: 91,35 mg alendronate sodium equivalent to 70 mg alendronic acid

Inactive ingredients: Colloidal anhydrous silica, croscarmellose sodium, magnesium stearate and microcrystalline cellulose.

Sugar free.

Pharmacological classification:

A 3.2 Connective tissue medicines, non-hormonal preparations

Pharmacological action:

Bisphosphonates are synthetic analogues of pyrophosphates that bind to the hydroxyapatite found in bone. Alendronate sodium is an aminobisphosphonate that acts as a specific inhibitor of osteoclast-mediated bone resorption.

Alendronate localises preferentially at sites of bone resorption, specifically under osteoclasts, and inhibits osteoclastic bone resorption with no direct effect on bone formation. During exposure to alendronate, normal bone is formed that incorporates alendronate into its matrix where it is pharmacologically inactive.

Pharmacokinetics:

Absorption:

The mean oral bioavailability of alendronate in women is 0,57 % for the 70 mg tablet when administered after an overnight fast and two hours before a standardised breakfast.

Bioavailability is decreased by 40 % when alendronate is given either 30 minutes or one hour before breakfast, when compared to taking the tablets two hours before eating.

Bioavailability is negligible whether alendronate is administered with or up to two hours after or before a standardised breakfast. When alendronate is taken with coffee or citrus juice, bioavailability is reduced by 60 %.

Distribution:

Alendronate is transiently distributed to soft tissue and then rapidly redistributed to bone or excreted in the urine. The volume of distribution is at least 28 l in humans.

Protein binding:

Approximately 78 % in human plasma.

Elimination:

Following a single intravenous dose of 10 mg alendronate, the renal clearance was 71 ml per minute. The systemic clearance was approximately 200 ml/min. After 6 hours the plasma concentrations fell by more than 95 %. The terminal half-life in humans is estimated to exceed 10 years, reflecting release of alendronate from the skeleton. There is no evidence that alendronate is metabolised in humans.

Indications:

ALENDRONATE 70 OETHMAAN is indicated in women for the treatment of post menopausal osteoporosis to reduce the risk of fractures, including those of the hip and spine (vertebral compression fractures).

Contra-indications:

- Hypersensitivity to alendronate or any other components of the formulation.
- Severe renal function impairment when creatinine clearance is less than 35 ml/minute.
- The risk factor should be considered when gastrointestinal problems such as duodenitis, dysphagia, gastritis, ulcers or symptomatic oesophageal diseases are present.
- Abnormalities of the oesophagus which delay oesophageal emptying such as stricture or achalasia.
- As alendronate may exacerbate hypocalcaemia or vitamin D deficiency, these conditions should be corrected before ALENDRONATE 70 OETHMAAN is administered.
- The inability to stand or sit upright for 30 minutes after taking the medicine.
- ***Paediatric age group***: Safety and efficacy have not been established.

- Pregnancy and lactation.
- A low energy stress fracture of the femur shaft while on Alendronate 70 Oethmaan, is a contraindication to restarting therapy. (see Warnings)

Warnings:

A dental examination with appropriate preventive dentistry should be considered prior to treatment with bisphosphonates, including ALENDRONATE 70 OETHMAAN, in patients with concomitant risk factors (e.g. cancer, chemotherapy, corticosteroids, poor oral hygiene).

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 is no data available to suggest whether discontinuation of bisphosphonate treatment reduces the risk of osteonecrosis of the jaw. Clinical judgement of the treating doctor should guide the management plan of each patient based on individual benefit/risk assessment.

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 ALENDRONATE 70 OETHMAAN-treated patients who have sustained a femoral shaft fracture. Poor healing of these fractures was also reported. Discontinuation of ALENDRONATE 70 OETHMAAN in patients with a stress fracture is recommended. (see Contraindications)

Interactions:

Other oral medications, such as calcium supplements and antacids, will interfere with the absorption of ALENDRONATE 70 OETHMAAN. Patients are advised to wait at least 30 minutes after ALENDRONATE 70 OETHMAAN before taking any other oral medication. No adverse experiences attributable to the concomitant use of alendronate and oestrogen (intravaginal, transdermal, or oral) in postmenopausal women have been identified.

The coadministration of ALENDRONATE 70 OETHMAAN with NSAID is associated with an increased risk of gastrointestinal irritation and gastric ulceration. Caution should be used during concomitant use.

Pregnancy and lactation:

ALENDRONATE 70 OETHMAAN use is contraindicated in pregnancy or lactation. (see Contraindications)

Dosage and directions for use:

It is important to take ALENDRONATE 70 OETHMAAN only as directed. The recommended dosage is one ALENDRONATE 70 OETHMAAN tablet (70 mg alendronic acid) once weekly, taken by mouth with a full glass of water, at least 2 hours before/after any food, beverages or other medication is taken. It is important to take ALENDRONATE 70 OETHMAAN with plain water only, as other beverages including mineral water are likely to reduce the absorption of alendronic acid. All patients should take calcium and vitamin D supplements if their diet is inadequate. These should be taken at least 30 minutes after taking ALENDRONATE 70 OETHMAAN. Remain in an upright position for 30 minutes after taking ALENDRONATE 70 OETHMAAN tablets. To facilitate delivery to the stomach and thus reduce the potential for oesophageal irritation, ALENDRONATE 70 OETHMAAN 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 70 OETHMAAN should not be taken at bedtime or before arising for the day. Failure to follow these instructions may increase the risk of oesophageal adverse experiences (see “Special Precautions”).

No dosage adjustment is necessary for the elderly or for patients with mild to moderate renal insufficiency (creatinine clearance 35 to 60 ml/min) (see “Contra-indications”).

Side Effects and Special Precautions:

Side Effects:

The following adverse reactions have been reported with alendronate:

Nervous system disorders:

Less frequently: Headache, Dysgeusia

Eye disorders:

Less frequently: Uveitis.

Gastrointestinal disorders:

Frequently: Abdominal pain, dyspepsia, oesophageal ulcer*, dysphagia*, abdominal distension, oesophagitis*, oesophageal erosions*, nausea, vomiting, constipation, diarrhoea, flatulence, acid regurgitation and melaena.

Less frequently: Oesophageal stricture*, oropharyngeal ulceration*, gastritis, gastric and duodenal ulcers, some severe and with complications, although a causal relationship has not been established.

(*see “Special precautions” and “Dosage and directions for use”).

Skin and subcutaneous tissue disorders:

Less frequently: Rash (occasionally with photosensitivity), erythema and alopecia.

Musculoskeletal, connective tissue and bone disorders:

Less frequently: Musculoskeletal (bone muscle or joint) pain. Stress fractures of the proximal femoral shaft. Osteonecrosis of the jaw (see "WARNINGS").

General disorders:

Less frequently: Hypersensitivity reactions, including urticaria and angioedema.

Of the above adverse experiences, abdominal pain was reported most commonly and incidences of the other adverse experiences did not exceed 4,1 %.

Laboratory test findings:

Less frequently: Asymptomatic, mild and transient decreases in serum calcium and phosphate have been observed.

Special Precautions:

Hypocalcaemia and vitamin D deficiency should be corrected before starting ALENDRONATE 70 OETHMAAN therapy, as ALENDRONATE 70 OETHMAAN may exacerbate these conditions.

The risk benefit should be considered in patients suffering from upper gastrointestinal diseases, such as dysphagia, duodenitis, gastritis, ulcers or symptomatic oesophageal conditions, because of possible irritant effects of ALENDRONATE 70 OETHMAAN on the upper gastrointestinal mucosa and a potential for worsening of the underlying disease.

In patients with known Barret’s oesphagus, ALENDRONATE 70 OETHMAAN is not recommended.

Oesophageal adverse experiences, such as oesophagitis, oesophageal ulcers and oesophageal erosions, infrequently followed by oesophageal stricture, have been reported in patients receiving treatment with ALENDRONATE 70 OETHMAAN. In some cases these have been severe and required hospitalisation.

Doctors should therefore be alert to any signs or symptoms signalling a possible oesophageal reaction and patients should be instructed to discontinue ALENDRONATE 70 OETHMAAN and seek medical attention if they develop dysphagia, odynophagia, retrosternal pain or new or worsening heartburn. The risk of severe

oesophageal adverse experiences appears to be greater in patients who lie down after taking ALENDRONATE 70 OETHMAAN and/or who fail to swallow it with a full glass of water and/or who continue to take ALENDRONATE 70 OETHMAAN after developing symptoms suggestive of oesophageal irritation. Therefore, it is very important that the full dosing instructions are provided to, and understood by; the patients (see "Dosage and directions for use").

To facilitate delivery to the stomach and thus reduce the potential for oesophageal irritation, patients should be instructed to swallow ALENDRONATE 70 OETHMAAN with a full glass of water and not lie down for at least 30 minutes and until after their first food of the day. Patients should not chew or suck on the tablet because of a potential for oropharyngeal ulceration.

Patients should be specifically instructed not to take ALENDRONATE 70 OETHMAAN at bedtime or before arising for the day. Patients should be informed that failure to follow these instructions may increase their risk of oesophageal problems. Patients should be instructed that if they develop symptoms of oesophageal disease (such as difficulty or pain upon swallowing, retrosternal pain or new or worsening heartburn) they should stop taking ALENDRONATE 70 OETHMAAN and consult their doctor.

Causes of osteoporosis other than oestrogen deficiency, aging and glucocorticoid use should be considered. Due to the positive effects of ALENDRONATE 70 OETHMAAN to increase 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.

Use in the elderly: There is no age-related difference in the efficacy or safety profiles of ALENDRONATE 70 OETHMAAN.

Effects on the ability to drive and use of machines: There are no data to suggest that ALENDRONATE 70 OETHMAAN affects the ability to drive or use machines

Known symptoms of overdosage and particulars of its treatment

Hypocalcaemia, hypophosphataemia and upper gastrointestinal adverse events, such as upset stomach, heartburn, oesophagitis, gastritis, or ulcer, may result from oral overdosage. The administration of milk and antacids may be of benefit. Because of the risk of oesophageal irritation, vomiting should not be induced. Keep the patient in an upright position.

Identification:

A white, round, biconvex film coated tablet debossed with "ALN 70" on one side.

Presentation:

4 tablets packed in aluminium foil blister packed in an outer cardboard carton.

Storage instructions:

Store below 25 °C in the original package. Protect from light and moisture. Keep the blisters in the carton until required for use.

KEEP OUT OF THE REACH OF CHILDREN

Registration number:

A 40/3.2/0514

Name and business address of the holder of the certificate of registration:

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