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

Excipients: Colloidal anhydrous silica, croscarmellose sodium, magnesium stearate and microcrystalline cellulose, lustre clear(coating).

Sugar free.

CATEGORY AND CLASS

A 3.2 Connective Tissue Medicines, Non-hormonal preparations

PHARMACOLOGICAL ACTION

Pharmacodynamic Properties

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 Properties:

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[illegible]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).

CONTRAINDICATIONS

- Hypersensitivity to alendronate or any other components of the formulation. (see COMPOSITION).
- 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 AND SPECIAL PRECAUTIONS)

WARNINGS AND SPECIAL PRECAUTIONS

Atypical fractures of the femur

Atypical, low energy fractures of the subtrochanteric and proximal femoral shaft have been reported with long-term use (usually longer than 3 years) in bisphosphonate-treated patients. Some were stress fractures (also reported as insufficiency fractures) occurring in the absence of apparent trauma. Some patients experienced prodromal pain in the affected area, often associated with imaging features of stress fracture, weeks to months before a fracture occurred. Approximately one third of these fractures were bilateral; therefore, the contralateral femur should be examined in patients who have sustained a femoral shaft stress fracture and receive appropriate orthopaedic care. Bisphosphonate treatment should be stopped in patients with stress fractures and they should receive appropriate orthopaedic care. (see CONTRAINDICATIONS)

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 receiving treatment regimens including primarily intravenous administered bisphosphonates. Many of these were receiving chemotherapy and corticosteroids. Osteonecrosis of the jaw has also been reported in patients with osteoporosis receiving oral bisphosphonates, such as **ALENDRONATE 70 OETHMAAN**.

A dental examination with appropriate preventive dentistry should be considered prior to treatment with bisphosphonates, such as **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, such as **ALENDRONATE 70 OETHMAAN**, 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.

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

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.

HUMAN REPRODUCTION

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 "CONTRAINDICATIONS").

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 "WARNINGS AND 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 AND SPECIAL PRECAUTIONS").

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.

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 at or 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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OETHMAAN BIOSIMS
It's gonna be okay

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