SCHEDULING STATUS

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1 NAME OF THE MEDICINE

FEMAX 70 mg (Tablets)

2 QUALITIVE AND QUANTITIVE COMPOSITION

Each tablet of FEMAX 70 contains 70mg alendronic acid as alendronic sodium trihydrate.

Contains sugar: Lactose monohydrate 142.64 mg

For full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

A white to off-white capsule shaped tablet embossed "AN 70" on one side and ">" (Arrow logo) on the other side.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

FEMAX (alendronate) is indicated:

- For the treatment of post-menopausal osteoporosis to reduce the risk of fractures, including those of the hip and spine (vertical compression fractures).
- For the treatment of primary hypogonadal osteoporosis in men and to reduce the risk of vertebral fractures.

4.2 Posology and method of administration

Posology

FEMAX must be taken at least 30 minutes before the first food, beverage or medication of the day. FEMAX should be taken with plain tap water only. Food and other beverages including mineral water may reduce absorption. FEMAX should be taken with a full glass of water and patients should not lie down for at least 30 minutes and until after their first meal. This is to facilitate delivery to the stomach and reduce the potential for oesophageal irritation. Do not take at bedtime or before rising for the day. Do not suck or chew the tablets.

Treatment of postmenopausal osteoporosis: 70 mg once weekly.

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Initial/ Date

Treatment of primary/hypogonadal osteoporosis in men: 70 mg once weekly. Patients should receive supplemental calcium and vitamin D if dietary intake is inadequate (see Special warnings and precautions for use).

Special populations

Elderly population:
No dosage adjustment is necessary in the elderly.

Renal impairment:
No dosage adjustment in patients with mild to moderate renal impairment (creatinine clearance 35 – 60 ml/min).

Method of administration

For oral use.

4.3 Contraindications

- Hypersensitivity to alendronate or any other component of the product
- Abnormalities of the oesophagus that delay oesophageal emptying such as stricture or achalasia (an oesophageal motility disorder)
- Inability to stand or sit upright for at least 30 minutes.
- Severe renal insufficiency (creatinine clearance< 35 ml/minute)
- Hypocalcaemia (see Special warnings and precautions for use)
- Pregnancy and lactation
- Paediatrics

4.4 Special warnings and precautions for use

- Fractures of the subtrochanteric and proximal shaft of the femur with minimal trauma (a fall from a standing height) after prolonged use (see Special warnings and precautions for use)
- Potential for oesophageal neoplastic change

Special Precautions

Low energy fractures of the femur

Initial/ Date

Low-energy fractures of the subtrochanteric and proximal femoral shaft have been reported in long-term (usually longer than three years) bisphosphonate-treated patients. Some were stress fractures (some of which were 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 complete 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. Biphosphonate therapy in patients with stress fractures should be discontinued.

FEMAX can cause local irritation to the mucous membrane in the upper part of the gastrointestinal tract.

As there is a risk of worsening of the underlying disease, caution should be observed if **FEMAX** is given to patients with active upper gastrointestinal tract problems, such as dysphagia, oesophageal disease (including known Barret's oesophagus), gastritis, duodenitis or ulcers, or in cases of recent (during the last year) severe gastrointestinal disease such as gastric ulcer, active gastrointestinal bleeding or surgery in the upper gastrointestinal tract other than pyloroplasty.

Oesophageal side effects (in some cases severe and requiring hospitalisation) such as oesophagitis, oesophageal ulcers or oesophageal erosions, in rare cases followed by oesophageal stricture, have been reported in patients receiving treatment with alendronate as in **FEMAX.**

The medical practitioner should therefore be alert to any signs or symptoms of possible oesophageal reaction. Patients should.be instructed to discontinue **FEMAX** and seek medical attention if they develop symptoms of oesophageal irritation such as dysphagia, pain on swallowing, retrosternal pain or new/worsened heartburn.

The risk of severe oesophageal side effects is thought to be greater in patients who do not take **FEMAX** correctly and/or continue to take **FEMAX** tablets after developing symptoms indicative of oesophageal irritation . It is very important that complete administration instructions are given to, and understood, by the patient (see *below and Dosage and directions for use). Patients should be informed that the risk of oesophageal problems may increase if they do not follow these instructions.

There have been post-marketing reports of gastric and duodenal ulcers, some of them severe and with complications. A causal connection cannot be excluded (see Undesirable effects).

Hypocalcaemia must be corrected before initiating therapy with **FEMAX** (see Contra- indications). Other disturbances of mineral metabolism (such as vitamin D deficiency) should also be effectively treated.
Causes of osteoporosis other than oestrogen deficiency, aging and glucocorticoid use should be investigated.
**To facilitate delivery to the stomach and thus minimise the risk of oesophageal reactions , patients should be instructed to swallow the tablets whole with a full glass of water , in an upright position (standing or sitting).*

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Initial/ Date

Tablets should be taken on rising for the day, on an empty stomach, at least 30 minutes before breakfast and any other medication. Patients should remain upright after taking the tablets and should not lie down before eating the first meal of the day. Patients should be instructed to not suck or chew the tablets because of a potential for orophyryngeal ulceration. 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 FEMAX and consult their medical practitioner.

Since NSAID use is associated with gastrointestinal irritation, caution is advised with the concomitant use of FEMAX and NSAIDs.
Localised osteonecrosis of the jaw (ONJ), generally associated with tooth extraction and/or local infection (including osteomyelitis) with delayed healing, has been reported with oral bisphosphonates (see ~~SIDE~~ UNDESIRABLE EFFECTS). Most reported cases of bisphosphonates-associated ONJ have been in cancer patients treated with intravenous bisphosphonates. Known risk factors for ONJ include a diagnosis of cancer, concomitant therapies (e.g., chemotherapy, radiotherapy, corticosteroids), poor oral hygiene, and co-morbid disorders (e.g., periodontal and /or other pre-existing dental disease, anaemia, coagulopathy, infection and smoking). Patients who develop ONJ should receive appropriate care by dental practitioner and discontinuation of bisphosphonate therapy should be considered based on individual benefit/risk assessment. Dental surgery may exacerbate the condition.
For patients requiring invasive dental surgery (e.g. tooth extraction, dental implants), clinical judgement of the prescribing medical practitioner and treating dental practitioner should guide the management plan, including FEMAX treatment, of each patient based on individual benefit/risk assessment.

Bone, joint, and/or muscle pain has been reported in patients taking bisphosphonates. In post-marketing experience, these symptoms have been severe and/or incapacitating (see SIDE UNDESIRABLE EFFECTS). The time to onset of symptoms varied from one day to several months after starting treatment. Most patients had relief of symptoms after stopping treatment. A subset had recurrence of symptoms when rechallenged with the same medicine or another bisphosphonate.

Milk or antacids should be administered to bind the alendronate. Due to the risk of oesophageal irritation, vomiting should not be induced and the patient should remain upright (sitting or standing).

Lactose warning:
FEMAX contains lactose monohydrate which may have an effect on the glycaemic control of patients with diabetes mellitus.
FEMAX contains lactose. Patients with the rare hereditary conditions of galactose intolerance e.g. galactosaemia, Lapp lactase deficiency, glucose-galactose malabsorption or fructose intolerance should not take FEMAX.

4.5 Interaction with other medicines and other forms of Interaction

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Initial/ Date

Concomitant administration of calcium supplements, iron or magnesium, including antacids and mineral supplements and some osmotic laxatives, will interfere with the absorption of FEMAX. Patients must wait at least 30 minutes after taking FEMAX before taking any other oral medication.

4.6 Fertility, pregnancy and lactation

Women of childbearing potential/ Contraception in males and females

No information available.

Pregnancy

FEMAX should not be administered to pregnant women (see Contraindications).

Breastfeeding

FEMAX should not be administered to lactating women (see Contraindications).

Fertility

No information available.

4.7 Effects on ability to drive and use machines

There are no data to suggest that **FEMAX 70** mg affects the ability to drive or use machines.

Initial/ Date

4.8 Undesirable effects

Tabulated list of adverse reactions

Body System	**Undesirable effect**		
	Frequent	Less frequent	Frequency not known
Immune system disorders:		Hypersensitivity reactions including urticaria and angio-oedema	
Metabolism and nutrition disorders:		Symptomatic hypocalcaemia generally in association with predisposing conditions	
Nervous system disorders:	Headache	Dizziness Vertigo Dysgeusia	
Eye disorders:		Uveitis Scleritis Episcleritis Diplopia with conjunctival swelling Eyelid oedema Non-specific conjunctivitis Blurred vision	
Cardiac disorders:		Increased risk of arterial fibrillation	
Gastrointes-tinal disorders:	Abdominal pain Dyspepsia Constipation Diarrhoea Flatulence Oesophageal ulcer Dysphagia Abdominal distention Acid regurgitation Oesophageal stricture	Nausea Gastritis Melaena Oropharyngeal ulceration Gastric or duodenal ulcers Oesophageal erosions Peptic ulceration Oesophagitis Oesophageal perforations	

Initial/ Date

Hepato-biliary disorders:		Hepatitis	
Skin and subcutaneous tissue disorders:		Rash Erythema Pruritus Isolated cases of severe skin reactions including Stevens-Johnson syndrome and toxic epidermal necrolysis Skin rash with photosensitivity Toxic epidermal necrolysis	
Musculoske-letal, connective tissue and bone disorders:	Bone, muscle and joint pain	Joint swelling Localised osteonecrosis of the jaw, generally associated with tooth extraction and/or local infection, with delayed healing Low-energy femoral shaft fracture	
General disorders and administra-tive site conditions:		Transient symptoms as in acute phase response (myalgia, malaise, asthenia and rarely fever), usually in association with initiation of treatment, peripheral oedema.	

Laboratory values:

In clinical trials, asymptomatic, slight transient decreases in serum calcium and serum phosphate were observed. Reductions in serum calcium < 2,0 mmol/l and serum phosphate to ≤ 0,65 mmol/l were seen in clinical trials.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions to SAHPRA via the "Report Drug Reaction Process", found online under SAHPRA's safety publications: https://www.sahpra.org.za/

Initial/ Date

4.9 Overdose

No specific information is available on the treatment of overdose of alendronate. Hypocalcaemia, hypophosphataemia and upper gastrointestinal side effects such as upset stomach, heartburn, oesophagitis, gastritis or ulcer may result from an oral overdosage. Milk or antacids, should be given to bind alendronate. Due to the risk of oesophageal irritation, vomiting should not be induced and the patient should remain fully upright.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

A.3.2 Connective tissue medicines, non hormonal preparations

Alendronic acid is a bisphosphonate. Bisphosphonates are synthetic analogues of pyrophosphate that bind to the hydroxyapatite found in bone. Alendronate sodium is a bisphosphonate that acts as a specific inhibitor of osteoclast-mediated bone resorption, possibly through inhibition of the mevalonate pathway. Since bone formation and bone resorption are coupled, bone formation is also reduced, but less so than resorption, leading to progressive gains in bone mass. The alendronate incorporated in the mineralised bone matrix is no longer pharmacologically active.

5.2 Pharmacokinetic properties

Absorption:
The oral bioavailability of alendronate is low (approximately 0,76 % of the oral dose) in post menopausal women when administered after an overnight fast and more than 2 hours before a standardised breakfast. Oral bioavailability in men is similar (average 0,6 %). On average , eating a standardised breakfast either 30 minutes or one hour after administration, decreased bioavailability by about 40 %. Taking alendronate either immediately or up to two hours after breakfast decreases bioavailability by between 85 and 90 %. Beverages such as coffee or orange juice decrease the bioavailability by approximately 60 % compared with water.

Distribution:
In humans, the mean steady state volume of distribution, excluding bone, is at least 28 litre.

Plasma concentrations following therapeutic oral doses are too low for analytical detection (less than 5 ng/ml). Protein binding in human plasma is approximately 78 %.

Metabolism:
Alendronate does not appear to be metabolised in animals or humans.

Elimination:
The sole route of elimination of alendronate is via the kidneys. Alendronate is also taken up and sequestered by the bone, from·where it is slowly released. Alendronate has a long terminal half-life(> 10 years) reflecting release from the skeleton.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Croscarmellose sodium
Lactose monohydrate
Magnesium stearate
Microcrystalline cellulose

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store at or below 25 °C in a dry place.
Store in the original package/container.
Keep the blister in the outer carton until required for use.
Keep out of reach of children.
Protect from moisture and light

6.5 Nature and contents of container

Blister packs (PVCPE/PVDC/Alu) of 4 tablets each are placed within a carton.

6.6 Special precautions for disposal of a used medicine or waste materials derived from such medicine and other handling of the product

No special requirements.

7 THE HOLDER OF THE CERTIFICATE OF REGISTRATION

Astral Pharma (Pty) Ltd
125 Meade Street
George
6529
South Africa

8 REGISTRATION NUMBER(S)

42/3.2/0221

Initial/ Date

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

19 April 2013

10 DATE OF REVISION OF TEXT

21 November 2022

Initial/ Date