

1. NAME OF THE MEDICINAL PRODUCT

Alendronate Sandoz 70 mg Film-coated Tablets.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains 70 mg alendronic acid (as sodium alendronate).

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablet.

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

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of post-menopausal osteoporosis.

Alendronate reduces the risk of vertebral and hip fractures.

4.2 Posology and method of administration

Posology

The recommended dose is one 70 mg tablet once weekly.

Use in elderly patients:

In clinical trials, there was no age-related difference with regard to efficacy or safety profiles of alendronate. Therefore no adjustment of the dose is necessary for elderly patients.

Use in impaired renal function:

No dose adjustment is necessary in patients with a glomerular filtration rate (GFR) greater than 35 ml/min. Alendronate is not recommended for patients with impaired renal function if the GFR is less than 35 ml/min, as there is no experience of this.

Use in impaired hepatic function:

No dose adjustment is necessary.

Use in children:

Alendronate has not been studied in children and should not be given to them.

Method of administration

For oral use.

To obtain satisfactory absorption of alendronate

Alendronate Sandoz 70 mg Film-coated tablets must be taken on an empty stomach immediately on rising in the morning, with plain water only, at least 30 minutes before the first food, drink or other medication of the day. Other drinks (including mineral water), food and some medicines are likely to reduce the absorption of alendronate (see section 4.5).

To assist delivery to the stomach and thus reduce the risk of irritation/side effects locally and in the oesophagus (see section 4.4).

- Alendronate Sandoz 70 mg Film-coated tablets should only be swallowed on arising for the day with a whole glass of water (not less than 200 ml or 7 fl.oz).
- Alendronate Sandoz 70 mg Film-coated tablets should be swallowed whole. Patients should not crush or chew the tablet or allow the tablet to dissolve in the mouth on account of the risk of oropharyngeal ulceration.
- Patients should not lie down until after the first meal of the day, which must be at least 30 minutes after taking the tablet.
- Patients should not lie down within 30 minutes of taking Alendronate Sandoz 70 mg Film-coated tablets.
- Alendronate Sandoz 70 mg Film-coated tablets should not be taken at bedtime or before arising for the day.

Patients should be given a calcium and vitamin D supplement if the diet is inadequate (see section 4.4).

Alendronate Sandoz 70 mg Film-coated tablets have not been investigated in the treatment of glucocorticoid-induced osteoporosis.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients.
- Abnormalities of the oesophagus and other factors that delay oesophageal emptying, such as stricture or achalasia.
- Inability to stand or sit upright for at least 30 minutes.
- Hypocalcaemia.

4.4 Special warnings and precautions for use

Upper gastrointestinal adverse reactions

Alendronate can cause local irritation to the upper gastrointestinal mucosa. Because there is a potential for worsening of the underlying disease, caution should be used when alendronate is given to patients with active upper gastrointestinal problems, such as dysphagia, oesophageal disease, gastritis, duodenitis, ulcers, with a recent history (within the previous year) of major gastrointestinal disease, such as peptic ulcer, or active gastro-intestinal bleeding, or surgery of the upper gastro-intestinal tract other than pyloroplasty (see section 4.3)

In patients with known Barrett's oesophagus, prescribers should consider the benefits and potential risks of alendronate on an individual patient basis.

Oesophageal reactions (sometimes severe and requiring hospitalisation), such as oesophagitis, oesophageal ulcers or oesophageal erosions, rarely followed by oesophageal stricture, have been reported in patients receiving alendronate. Physicians should therefore be alert to any signs or symptoms signaling a possible oesophageal reaction and patients should be instructed to discontinue alendronate and seek medical attention if they develop symptoms of oesophageal irritation, such as dysphagia, pain on swallowing, retrosternal pain new or worsening heartburn.

The risk of severe oesophageal adverse experiences appears to be greater in patients who fail to take alendronate correctly and/or who continue to take alendronate after developing symptoms suggestive of oesophageal irritation. It is very important that the full dosing instructions are provided to, and understood by the patient (see section 4.2). Patients should be informed that failure to follow these instructions may increase their risk of oesophageal problems.

While no increased risk was observed in extensive clinical trials, there have been reports of rare (postmarketing) reports of gastric and duodenal ulcers, some severe and with complications.

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 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.

The following risk factors should be considered when evaluating an individual's risk of developing osteonecrosis of the jaw:

- potency of the bisphosphonate (highest for zoledronic acid), route of administration (see above) and cumulative dose
- cancer, chemotherapy, radiotherapy, corticosteroids, angiogenesis inhibitors, smoking
- a history of dental disease, poor oral hygiene, periodontal disease, invasive dental procedures and poorly fitting dentures.

A dental examination with appropriate preventive dentistry should be considered prior to treatment with bisphosphonates in patients with poor dental status.

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 judgement 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.

Osteonecrosis of the external auditory canal has been reported with bisphosphonates, mainly in association with long-term therapy. Possible risk factors for osteonecrosis of the external auditory canal include steroid use and chemotherapy and/or local risk factors such as infection or trauma. The possibility of osteonecrosis of the external auditory canal should be considered in patients receiving bisphosphonates who present with ear symptoms including chronic ear infections.

Musculoskeletal pain

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 (see section 4.8). 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 medicinal product or another bisphosphonate.

Atypical fractures of the femur

Atypical subtrochanteric and diaphyseal femoral fractures have been reported with bisphosphonate therapy, primarily in patients receiving long-term treatment for osteoporosis. These transverse or short oblique fractures can occur anywhere along the femur from just below the lesser trochanter to just above the supracondylar flare. These fractures occur after minimal or no trauma and some patients experienced thigh or groin pain, often associated with imaging features of stress fractures, weeks to months before presenting with a completed femoral fracture. Fractures are 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 suspected to have an atypical femur fracture should be considered 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.

Skin reactions

In post-marketing experience, there have been rare reports of severe skin reactions including Stevens Johnson syndrome and toxic epidermal necrolysis.

Additionally for Alendronate Sandoz 70mg

Missed dose

Patients should be instructed that if they miss a dose of alendronate 70 mg once weekly formulation, 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.

Renal impairment

Alendronate is not recommended for patients with renal impairment where creatinine clearance is less than 35 ml/min (see section 4.2).

Causes of osteoporosis other than oestrogen deficiency and ageing should be considered.

Bone and mineral metabolism

Hypocalcaemia must be corrected before initiating therapy with alendronate (see section 4.3). 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 hypocalcaemia should be monitored during therapy with alendronate.

Due to the positive effects of alendronate in increasing bone mineral, decreases in serum calcium and phosphate may occur especially in patients taking glucocorticoids in whom calcium absorption may be decreased. These are usually small and asymptomatic. However, there have been rare reports of symptomatic hypocalcaemia, 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.

4.5 Interactions with other medicinal products and other forms of interaction

If taken at the same time, it is likely that foods and drinks (including mineral water), calcium supplements, antacids and some oral medicines will interfere with the absorption of alendronate. Therefore, patients must wait at least 30 minutes after taking alendronate before taking any other oral medicinal product (see sections 4.2 and 5.2).

No other interactions with medicinal products of clinical significance are anticipated. A number of patients in the clinical trials received oestrogen (intravaginally, transdermally or oral) while taking alendronate. 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 alendronate was used concomitantly with a wide range of commonly prescribed medicinal products without evidence of clinical adverse interactions.

4.6 Pregnancy and lactation

Pregnancy

There are no or limited amount of data from the use of alendronate in pregnant women. Alendronate should not be used during pregnancy.

Breast-feeding

It is unknown whether alendronate/metabolites are excreted in human milk. A risk to the newborns/infants cannot be excluded. Alendronate should not be used during breast-feeding.

Fertility

Bisphosphonates are incorporated into the bone matrix, from which they are gradually released over a period of years. The amount of bisphosphonate incorporated into adult bone, and hence, the amount available for release back into the systemic circulation, is directly related to the dose and duration of bisphosphonate use (see section 5.2). There are no data on foetal risk in humans. However, there is a theoretical risk of foetal harm, predominantly skeletal, if a woman becomes pregnant after completing a course of bisphosphonate therapy to conception, the particular bisphosphonate used, and the route of administration (intravenous versus oral) on the risk has not been studied.

4.7 Effects on ability to drive and use machines

Alendronate has no or negligible direct influence on the ability to drive and use machines. However, certain adverse reactions that have been reported with alendronate may affect some patients' ability to drive or operate machinery. Individual responses to alendronate may vary (see section 4.8).

4.8 Undesirable effects

List of adverse reactions

The following undesirable effects have also been reported in clinical studies and/or post marketing use: Frequencies are defined as very common, common, uncommon, rare and very rare.

Immune system disorders

Rare: Hypersensitivity reactions including urticaria and angioedema

Metabolism and nutrition disorders

Rare: Symptomatic hypocalcaemia, often in association with predisposing conditions[§]

Nervous system disorders

Common: Headache, dizziness[†]

Uncommon: Dysgeusia[†]

Eye disorders

Uncommon: Eye inflammation (uveitis, scleritis, episcleritis)

Ear and labyrinth disorders

Common: Vertigo[†]

Gastrointestinal disorders

Common: Abdominal pain, dyspepsia, constipation, diarrhoea, flatulence, oesophageal ulcer*, dysphagia*, abdominal distension, acid regurgitation
Uncommon: Nausea, vomiting, gastritis, oesophagitis*, oesophageal erosions*, melaena†
Rare: Oesophageal stricture*, oropharyngeal ulceration*, upper gastrointestinal PUBs (perforation, ulcers, bleeding)§

Skin and subcutaneous tissue disorders

Common: Alopecia†, pruritus†
Uncommon: Rash, erythema
Rare: Rash with photosensitivity, severe skin reactions including Stevens-Johnson syndrome and toxic epidermal necrolysis†

Musculoskeletal and connective tissue disorders

Very common: Musculoskeletal (bone, muscle or joint) pain which is sometimes severe†§
Common: Joint swelling†
Rare: Osteonecrosis of the jaw‡§; atypical subtrochanteric and diaphyseal femoral fractures (bisphosphonate class adverse reaction)⊥
Very rare: Osteonecrosis of the external auditory canal (bisphosphonate class adverse reaction)

General disorders and administration site conditions

Common: Asthenia†, peripheral oedema†
Uncommon: Transient symptoms as in an acute phase response (myalgia, malaise and rarely, fever), typically in association with initiation of treatment†

§ See section 4.4

† Frequency in clinical trials was similar in the medicinal product and placebo group.

* See sections 4.2 and 4.4

‡ This adverse reaction was identified through post-marketing surveillance. The frequency of rare was estimated based on relevant clinical trials.

⊥ Identified in postmarketing experience

4.8 Overdose

Symptoms

Hypocalcaemia, hypophosphataemia and upper gastrointestinal adverse events, such as upset stomach, heartburn, oesophagitis, gastritis, or ulcer, may result from oral overdose.

Management

No specific information is available on the treatment of overdose with alendronate. Milk or antacids should be given to bind alendronate. Owing 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

Pharmacotherapeutic group: Drugs for treatment of bone diseases, drugs affecting bone structure and mineralisation, bisphosphonates.

ATC code: M05BA04

The active substance in Alendronate Sandoz 70 mg Film-coated tablets, sodium alendronate trihydrate, is a bisphosphonate that inhibits osteoclastic bone resorption without any direct effect on bone formation. There is a preference for localisation of alendronate to sites where active resorption takes place. Osteoclastic activity is inhibited, but formation and binding of the osteoclasts is not affected. Bone formed during treatment with alendronate is of normal quality.

Paediatric patients

Results are insufficient to support the use of alendronate sodium in paediatric patients with osteogenesis imperfecta.

5.2 Pharmacokinetic properties

Absorption

The mean oral bioavailability of alendronate in women was 0.64% for doses ranging from 5 to 70 mg given after an overnight fast and two hours before a standardised breakfast. Bioavailability decreased to an estimated 0.46% and 0.39% when alendronate was given an hour or half an hour before a

standardised breakfast. Alendronate was effective when it was given at least 30 minutes before the first meal or drink of the day. Bioavailability was negligible irrespective of whether alendronate was given together with or up to two hours after a standardised breakfast. Concomitant administration of alendronate with coffee or orange juice reduced bioavailability by approx. 60%. Oral prednisolone (20 mg three times daily for five days) did not result in any clinically meaningful change in the oral bioavailability of alendronate.

Distribution

The mean steady-state volume of distribution, exclusive of bone, is at least 28 litres in humans. Concentrations of active substance 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 metabolised in animals or humans.

Elimination

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 thought to interfere with the excretion of other drugs by those systems in humans.

Characteristics in patients

The drug that is not deposited in bone is rapidly excreted in the urine. Although no clinical information is available, it is likely that, as in animals, elimination of alendronate via the kidney will be reduced in patients with impaired renal function. Therefore, somewhat greater accumulation of alendronate in bone might be expected in patients with impaired renal function (see section 4.2).

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core:

Microcrystalline cellulose
Colloidal anhydrous silica
Croscarmellose sodium
Magnesium stearate

Tablet coating:

Carrageenan
Microcrystalline cellulose
Macrogol

6.2 Incompatibilities

Not applicable.

6.3 Shelf-life

3 years.

6.4 Special precautions for storage

Do not store above 30°C. Store in the original package.

6.5 Nature and contents of container

The product is packed in OPA-Aluminium-PVC/aluminium blister and may be supplied in the following pack sizes:
4 film-coated tablets.

6.6 Special precautions for disposal and other handling

No special requirements.

7. PRODUCT REGISTRATION HOLDER

Sandoz Products Malaysia Sdn. Bhd.
3A-2 & 3A-3, Level 3A, Menara KEN TTDI,
No. 37, Jalan Burhanuddin Helmi, Taman Tun Dr Ismail,
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8. DATE OF REVISION OF THE TEXT

Jul 2026