Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Fostepor Once Weekly 70mg tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 70 mg alendronic acid as sodium alendronate.

Excipient with known effect:
Each tablet contains 150.94 mg lactose (as lactose monohydrate).

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablet.

White, bi-convex tablet, embossed AD70 on one side and G on the reverse.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of postmenopausal osteoporosis.
Alendronate reduces the risk of vertebral fractures as well as hip fractures.

4.2 Posology and method of administration

Posology

The recommended dosage is one 70mg tablet once weekly. The optimal duration of bisphosphonate treatment for osteoporosis has not been established. The need for continued treatment should be re-evaluated periodically based on the benefits and potential risks of Fostepor Once Weekly on an individual patient basis, particularly after 5 or more years of use.

Special populations
Elderly
In clinical studies there was no age-related difference in the efficacy or safety profiles of alendronate. Therefore, no dosage adjustment is necessary for the elderly .

Patients with renal impairment:
No dosage adjustment is necessary for patients with creatinine clearance greater than 35 ml/min. Alendronate is not recommended for patients with renal impairment where creatinine clearance is less than 35 ml/min, due to lack of experience.

Paediatric population:
The safety and efficacy of alendronate sodium (the active substance) in children in less than 18 years of age has not been established. This medical product should not be used in children less 18 years of age. Currently available data for alendronic acid in the paediatric population is described in section 5.1.

Method of administration

For oral administration

To permit adequate absorption of alendronate:

Fostepor Once Weekly must be taken at least 30 minutes before the first food, beverage, or medicinal product of the day with plain water only. Other beverages (including mineral water), food and some medicinal products are likely to reduce the absorption of alendronate (see section 4.5).

To facilitate delivery to the stomach and thus reduce the potential for local and oesophageal irritation/adverse experiences (see section 4.4):

• Fostepor Once Weekly should only be swallowed upon arising for the day with a full glass of water (not less than 200 ml).

• Patients should only swallow Fostepor Once Weekly whole. Patients should not crush or chew the tablet or allow the tablet to dissolve in their mouths because of a potential for oropharyngeal ulceration.

• Patients should not lie down until after their first food of the day which should be at least 30 minutes after taking the tablet.

• Patients should not lie down for at least 30 minutes after taking Fostepor Once Weekly.

• Fostepor Once Weekly should not be taken at bedtime or before arising for the day.

Patients should receive supplemental calcium and vitamin D if dietary intake is inadequate (see section 4.4).

Alendronate in a dosage of 70 mg once weekly has not been investigated in the treatment of glucocorticoid-induced osteoporosis.

4.3 Contraindications

● Abnormalities of the oesophagus and other factors which delay oesophageal emptying such as stricture or achalasia.
● Inability to stand or sit upright for at least 30 minutes.
● Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
● Hypocalcaemia.

(see also section 4.4)

4.4 Special warnings and precautions for use

Upper gastrointestinal adverse reactions
Alendronate can cause local irritation of the upper gastro-intestinal 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 gastro-intestinal problems, such as dysphagia, oesophageal disease, gastritis, duodenitis, ulcers, or with a recent history (within the previous year) of major gastro-intestinal disease such as peptic ulcer, or active gastro-intestinal bleeding, or surgery of the upper gastrointestinal 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 and oesophageal erosions, rarely followed by oesophageal stricture, have been reported in patients receiving alendronate. Physicians should therefore be alert to any signs or symptoms signalling 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 or retrosternal pain, new or worsening heartburn (see section 4.8).

The risk of severe oesophageal adverse experiences appears to be greater in patients who fail to take alendronate properly 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 rare (post-marketing) reports of gastric and duodenal ulcers, some severe and with complications (see section 4.8).

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 who are 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 oral 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
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 such as pain or discharge, or chronic ear infections.

Musculosketal 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 treatment. 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 experience thigh or groin pain, often associated with imaging features of stress fractures, weeks to months before presenting with a complete 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 has also been reported.

Discontinuation of bisphosphonate therapy in patients suspected to have an atypical femur fracture should be considered 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 reaction
In post-marketing experience, there have been rare reports of severe skin reactions including Stevens-Johnson syndrome and toxic epidermal necrolysis

Missed dose

Patients should be instructed that if they miss a dose of Fostepor Once Weekly, 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 per 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).

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

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 before starting this medicinal product. In patients with these conditions, serum calcium and symptoms of hypocalcaemia should be monitored during therapy with Fostepor Once Weekly.

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.

Excipients
This medicinal product contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

This medicinal product contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

If taken at the same time, it is likely that food and beverages (including mineral water), calcium supplements, antacids, and some oral medicinal products will interfere with 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 drug interactions with medicinal products of clinical significance are anticipated. A number of patients in the clinical trials received oestrogen (intravaginal, transdermal, 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 Fertility, pregnancy and lactation

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

Studies in animals have shown reproductive toxicity. Alendronate given during pregnancy in rats caused dystocia related to hypocalcaemia (see section 5.3).

Breast-feeding
It is not known whether alendronate/metabolites are excreted into human breast milk. A risk to the new-borns/infants cannot be excluded. Alendronate should not be used by breast-feeding women.

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. The impact of variables such as time between cessation 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. Patients may experience certain adverse reactions (for example blurred vision, dizziness and severe bone, muscle or joint pain (see section 4.8) that may influence the ability to drive and use machines.

4.8 Undesirable effects

Summary of the safety profile

In a one-year study in post-menopausal women with osteoporosis the overall safety profiles of alendronate Once Weekly 70 mg (n=519) and alendronate 10 mg/day (n=370) were similar.

In two three-year studies of virtually identical design, in post-menopausal women (alendronate 10 mg: n=196, placebo: n=397) the overall safety profiles of alendronate 10 mg/day and placebo were similar.

Adverse experiences reported by the investigators as possibly, probably or definitely drug-related are presented below if they occurred in ≥1% in either treatment group in the one-year study, or in ≥1% of patients treated with alendronate 10 mg/day and at a greater incidence than in patients given placebo in the three-year studies:

	One-Year Study		Three-Year Studies	
	Alendronate once weekly 70 mg (n=519) %	Alendronate 10 mg/day (n=370) %	Alendronate 10 mg/day (n=196) %	Placebo (n=397) %
Gastro-intestinal				
Abdominal pain	3.7	3.0	6.6	4.8
Dyspepsia	2.7	2.2	3.6	3.5
Acid regurgitation	1.9	2.4	2.0	4.3
Nausea	1.9	2.4	3.6	4.0
Abdominal distension	1.0	1.4	1.0	0.8
Constipation	0.8	1.6	3.1	1.8
Diarrhoea	0.6	0.5	3.1	1.8
Dysphagia	0.4	0.5	1.0	0.0
Flatulence	0.4	1.6	2.6	0.5
Gastritis	0.2	1.1	0.5	1.3
Gastric ulcer	0.0	1.1	0.0	0.0
Oesophageal ulcer	0.0	0.0	1.5	0.0
Musculoskeletal				
musculoskeletal (bone, muscle or joint) pain	2.9	3.2	4.1	2.5
Muscle cramp	0.2	1.1	0.0	1.0
Neurological				
Headache	0.4	0.3	2.6	1.5

Tabulated list of adverse reactions

The following adverse experiences have also been reported during clinical studies and/or post-marketing use:

Frequencies are defined as: [Very common (≥1/10), Common (≥1/100 to < 1/10), Uncommon (≥1/1,000 to < 1/100), Rare (≥1/10,000 to <1/1,000), Very rare (< 1/10,000)]

System Organ Class	Frequency	Adverse Experience Term
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 drug 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.*

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via HPRA Pharmacovigilance, Earlsfort Terrace, IRL – Dublin 2; Tel:+353 1 6764971; Fax: +353 1 6762517; Website: www.hpra.ie; e-mail: medsafety@hpra.ie.

4.9 Overdose

Symptoms

Hypocalcaemia, hypophosphataemia and upper gastro-intestinal symptoms, 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:
Bisphosphonates for the treatment of bone diseases.
ATC code: M05BA04

Mechanism of action
The active ingredient of Fostepor Once Weekly, sodium alendronate trihydrate, is a bisphosphonate which inhibits the bone resorption of osteoclasts with no direct effect on the bone formation. Preclinical investigations have demonstrated that alendronate is primarily located in places with active resorption. The osteoclast activity is inhibited, but recruitment and attachment of osteoclasts are not affected. The bone mass formed during treatment with alendronate has a normal structure.

Clinical efficacy and safety
Treatment of post-menopausal osteoporosis:
Osteoporosis is defined as BMD (bone mass density) in the spine or the hip 2.5 SD below the average value of a normal, younger population or as a previous fragility fracture regardless of the BMD.

The therapeutic equivalence of alendronate 70 mg once weekly (n=519) and alendronate 10 mg daily (n=370) was demonstrated in a one-year multicenter study of post-menopausal women with osteoporosis. Average increases from baseline in columna lumbalis BMD following one year was 5.1% (95% CI: 4.8; 5.4%) in the 70 mg group and 5.4% (95% CI: 5.0; 5.8%) in the 10 mg group. Average increases in BMD in the treatment groups of 70 mg once weekly and 10 mg once daily were 2.3% and 2.9%, respectively, in collum femoris and 2.9% and 3.1%, respectively, in the whole hip. The two treatment groups were also similar with regard to BMD increases at other skeletal sites.

The alendronate effect on BMD and fracture incidence in post-menopausal women was investigated in two, identically designed, initial-effect-studies (n=994) and in the study "Fracture Intervention Trial" (FIT: n=6,459).

Following three years of treatment with alendronate 10 mg daily in the initial-effect-studies average increases in bone mineral density (BMD) of 8.8%; 5.9% and 7.8%, respectively, were observed in columna spinalis, collum femoris and trochanter as compared to placebo. Total BMD was also significantly increased. Of patients treated with alendronate 48% fewer experienced one or more vertebral fractures (alendronate 3.2% versus placebo 6.2%) as compared with patients treated with placebo. In the two-year extension of these studies a continued increase of BMD in columna spinalis and trochanter was observed. BMD in collum femoris and total BMD were preserved.

FIT consisted of two placebo-controlled studies with alendronate (5 mg daily for two years and 10 mg daily for further one or two years):

● **FIT 1**: A three-year investigation of 2,027 patients having at least one vertebral (compression) fracture at baseline. In this study alendronate once daily reduced the incidence of ≥1 new vertebral fracture by 47% (alendronate 7.9% versus placebo 15.0%). Furthermore, a statistically significant reduction of the hip fracture incidence was demonstrated (1.1% versus 2.2%, a reduction of 51%).

●**FIT 2**: A four-year investigation of 4,432 patients with a low bone mass but with no vertebral fracture at baseline. An analysis of the subgroup of osteoporotic women (37% of the global population who had osteoporosis corresponding to the above definition) demonstrated a significant difference of the incidence of hip fractures (alendronate 1.0% versus placebo 2.2%, a reduction of 56%) and of the incidence of ≥1 vertebral fracture (2.9% versus 5.8%, a reduction of 50%).

Laboratory test findings
In clinical studies, asymptomatic, mild and transient decreases in serum calcium and phosphate were observed in approximately 18 and 10%, respectively, of patients taking alendronate 10 mg/day versus approximately 12 and 3% of those

taking placebo. However, the incidences of decreases in serum calcium to <8.0 mg/dl (2.0 mmol/l) and serum phosphate to ≤2.0 mg/dl (0.65 mmol/l) were similar in both treatment groups.

Paediatric population
Alendronate sodium has been studied in a small number of patients with osteogenesis imperfecta under the age of 18 years. Results are insufficient to support the use of alendronate sodium in paediatric patients with osteogenesis imperfecta.

5.2 Pharmacokinetic properties

Absorption
As compared to intravenous reference dose, the oral mean bioavailability of alendronate is 0.64% in women at doses from 5-70 mg when administered after one night's fast and two hours prior to a standard breakfast. The bioavailability was reduced to approximately 0.46% and 0.39% when alendronate was administered one hour or half an hour prior to a standard breakfast. In the osteoporosis studies alendronate was effective when administered at least 30 minutes prior to the first meal or the first drinks of the day.

Bioavailability was negligible regardless of whether alendronate was taken together with or up to two hours after a standard breakfast. Coffee and orange juice reduced the bioavailability by approximately 60%.

In healthy volunteers oral prednisone (20 mg thrice daily for five days) did not change the bioavailability of alendronate significantly (average increase from 20-44%).

Distribution
Rat studies show that alendronate is transiently distributed to soft tissue following administration of 1 mg/kg, but then it is fast redistributed to the bones or excreted with urine. Average steady state distribution volume, excluding bones, is at least 28 litres in human beings. Plasma concentrations of the medicinal product following administration of an oral therapeutic dose is below detection limit (<5 ng/ml). The protein binding in human plasma is approximately 78%.

Biotransformation
There are no signs that alendronate is metabolised in animals or human beings.

Elimination
Following a single intravenous dose [14C] alendronate, approximately 50% of radioactivity is excreted via urine within 72 hours. Very little or no radioactivity is recovered in faeces. Renal clearance is 71 ml/minute after a single dose of 10 mg IV and systemic clearance does not exceed 200 ml/min. Within six hours the plasma concentration declines by more than 95% following IV administration. Based on the slow release of alendronate from the skeleton, half-life in humans is estimated to be>10 years. In rats alendronate is not excreted via the acid or base transportation systems of the kidneys and thus it is not expected to interfere with excretion of other drugs via these systems in human beings.

Renal impairment
Preclinical investigations show that a medicinal product that is not deposited in the bone, is rapidly excreted in the urine. Following chronic dosage of cumulative IV doses of up to 35 mg/kg in animals, no saturation of bone uptake has been demonstrated. As in animals it is probable that the elimination of alendronate via the kidneys will be reduced in renally insufficient patients. However, there are no clinical data available on this. Consequently, a larger accumulation of alendronate in bones may be expected in humans with a reduced renal function (see section 4.2).

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity and carcinogenic potential. Studies in rats have shown that treatment with alendronate during pregnancy was associated with dystocia in dams during parturition which was related to hypocalcaemia. In studies, rats given high doses showed an increased incidence of incomplete foetal ossification. The relevance to humans is unknown.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Cellulose, microcrystalline

Lactose monohydrate
Croscarmellose sodium
Magnesium stearate
Povidone

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

Clear or green, opaque PVC/aluminium blister packs containing 4, 8 or 12 tablets.

Polypropylene tablet container with polyethylene cap and optional polyethylene ullage filler containing 4, 8, 12 or 100 (dispensing pack) tablets.

*Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements for disposal.

7 MARKETING AUTHORISATION HOLDER

Viatris Limited
Damastown Industrial Park
Mulhuddart
Dublin 15
Dublin
Ireland

8 MARKETING AUTHORISATION NUMBER

PA23266/018/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 13 October 2006
Date of last renewal: 19 May 2010

10 DATE OF REVISION OF THE TEXT

March 2024