OSTEONATE PLUS ONCE A WEEK

SCHEDULING STATUS S3

1. NAME OF THE MEDICINE
OSTEONATE PLUS 2800 ONCE A WEEK tablets.
OSTEONATE PLUS 5600 ONCE A WEEK tablets.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
OSTEONATE PLUS 2800 ONCE A WEEK: Each tablet contains sodium alendronate trihydrate equivalent to 70 mg alendronic acid and cholecalciferol concentrate (powder form) equivalent to 70 mcg cholecalciferol (2800 IU Vitamin D_3).
OSTEONATE PLUS 5600 ONCE A WEEK: Each tablet contains sodium alendronate trihydrate equivalent to 70 mg alendronic acid and cholecalciferol concentrate (powder form) equivalent to 140 mcg cholecalciferol (5600 IU vitamin D_3).

OSTEONATE PLUS ONCE A WEEK contains sugar (lactose and sucrose) in the following quantities, respectively:
OSTEONATE PLUS 2800 ONCE A WEEK: 87,140 mg; 13,745 mg
OSTEONATE PLUS 5600 ONCE A WEEK: 59,140 mg; 27,490 mg

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM
Tablets.
OSTEONATE PLUS 2800 ONCE A WEEK: White to off-white oblong, biconvex tablets, mottled, engraved with 2800 on one side with dimensions 12,3 mm ± 0,2 mm in length and 6,5 ± 0,2 mm in width.
OSTEONATE PLUS 5600 ONCE A WEEK: White to off-white, modified rectangle-shaped tablets, mottled, engraved with 5600 on one side with dimensions 11,4 mm ± 0,2 mm in length and 7,2 ± 0,2 mm in width.

4. CLINICAL PARTICULARS
4.1 Therapeutic indications
OSTEONATE PLUS ONCE A WEEK is indicated in women for the treatment of postmenopausal osteoporosis to reduce the risk of fractures, including those of the hip and spine (vertebral compression fractures) and to help ensure vitamin D adequacy.

4.2 Posology and method of administration
Posology
The recommended dosage is 1 (one) OSTEONATE PLUS ONCE A WEEK tablet once a week. For osteoporotic patients receiving a separate vitamin D supplement (400 IU) daily, the appropriate dose of OSTEONATE PLUS ONCE A WEEK is 70mg/2800 IU once weekly.

Patients should receive supplemental calcium and/or vitamin D if intake is inadequate (see section 4.4). Doctors should consider the vitamin D intake of the individual patient from vitamins and dietary supplements. OSTEONATE PLUS ONCE A WEEK provides a week's supply of vitamin D, based on a daily dose of 400 IU and 800 IU respectively, in a single once-a-week dose.

Special populations
Elderly
No dosage adjustment is necessary for the elderly.

Renal insufficiency
No dosage adjustment is necessary for patients with mild-to-moderate renal insufficiency (creatinine clearance 35 to 60 mL/min) (see section 4.3 and 5.2).
In patients with severe renal insufficiency, OSTEONATE PLUS ONCE A WEEK is contraindicated (see section 4.3).

Paediatric population
The safety and efficacy of OSTEONATE PLUS ONCE A WEEK in children less than 18 years of age have not been established.
OSTEONATE PLUS ONCE A WEEK is therefore contraindicated in children below 18 years (see section 4.3).

Method of administration
Oral use.
To facilitate delivery to the stomach and to reduce the potential for oesophageal irritation, OSTEONATE PLUS ONCE A WEEK must be taken at least a ½ hour before the first food, beverage or medication of the day, with a full glass of plain water.
Patients should only swallow OSTEONATE PLUS ONCE A WEEK 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 (see section 4.4).

Other beverages (including mineral water), food and some medicines are likely to reduce the absorption of alendronate, an active ingredient of OSTEONATE PLUS ONCE A WEEK (see section 4.5). Patients should not lie down for at least 30 minutes and not until after they have eaten. OSTEONATE PLUS ONCE A WEEK 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 section 4.4).

4.3 Contraindications
- hypersensitivity to alendronate, cholecalciferol or to any of the ingredients of OSTEONATE PLUS ONCE A WEEK
- abnormalities of the oesophagus which delay oesophageal emptying such as stricture or achalasia
- inability to stand or sit upright for at least 30 minutes
- hypocalcaemia (see section 4.4)
- severe renal insufficiency (creatinine clearance less than 35 mL/min)
- pregnancy and lactation (see section 4.6)
- children below the age of 18 years.

4.4 Special warnings and precautions for use
Alendronic acid
Upper gastrointestinal adverse reactions
OSTEONATE PLUS ONCE A WEEK may cause local irritation of the upper gastro-intestinal mucosa.

Oesophageal adverse experiences, such as oesophagitis, oesophageal ulcers and oesophageal erosions, which may be followed by oesophageal stricture or perforation, have been reported in patients receiving treatment with alendronate, as contained in OSTEONATE PLUS ONCE A WEEK. 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 OSTEONATE PLUS ONCE A WEEK 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 OSTEONATE PLUS ONCE A WEEK and/or who fail to swallow it with a full glass of water, and/or who continue to take OSTEONATE PLUS ONCE A WEEK after developing symptoms suggestive of oesophageal irritation.

It is therefore very important that the full dosing instructions are provided to, and understood by, the patient (see section 4.2).

Although no increased risk has been observed, there have been reports of gastric and duodenal ulcers, some severe and with complications when taking alendronate, as contained in OSTEONATE PLUS ONCE A WEEK (see section 4.8).

Due to possible irritant effects of alendronate, as contained in OSTEONATE PLUS ONCE A WEEK, on the upper gastro-intestinal mucosa and a potential for worsening of the underlying disease, caution should be used when OSTEONATE PLUS ONCE A WEEK is given to patients with active upper gastro-intestinal problems, such as dysphagia, oesophageal diseases (including known Barrett's oesophagus), gastritis, duodenitis or ulcers, or with a recent history (within the previous year) of major gastrointestinal disease such as peptic ulcer, or active gastrointestinal bleeding, or surgery of the upper gastrointestinal tract other than pyloroplasty (see section 4.3).

To facilitate delivery to the stomach and therefore reduce the potential for oesophageal irritation, patients should be instructed to swallow OSTEONATE PLUS ONCE A WEEK with a full glass of water and to not lie down for at least 30 minutes and not until they have eaten. Patients should not chew or suck on the tablet because of a potential for oropharyngeal ulceration. Patients should be specifically instructed not to take OSTEONATE PLUS ONCE A WEEK 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 OSTEONATE PLUS ONCE A WEEK and consult their doctor.

Since nonsteroidal anti-inflammatory medicine (NSAID) use is associated with gastrointestinal irritation, caution is advised with the concomitant use of OSTEONATE PLUS ONCE A WEEK and NSAIDs.

Osteonecrosis of the jaw:
Osteonecrosis of the jaw, generally associated with tooth extraction and/or local infection (including osteomyelitis) with delayed healing, has been reported, mainly 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 OSTEONATE PLUS ONCE A WEEK.
A dental examination with appropriate preventative dentistry should be considered prior to treatment with bisphosphonates, such as OSTEONATE PLUS ONCE A WEEK, in patients with concomitant risk factors. Known risk factors for osteonecrosis of the jaw include a diagnosis of cancer, concomitant therapies (e.g. chemotherapy, radiotherapy, corticosteroids, angiogenesis inhibitors), poor oral hygiene and co-morbid disorders (e.g. periodontal and/or other pre-existing dental disease, poorly fitting dentures, anaemia, coagulopathy, infection and smoking).

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 OSTEONATE PLUS ONCE A WEEK, dental surgery may exacerbate the condition.
For patients requiring invasive dental procedures (e.g. tooth extraction, dental implants), 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 an 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.

Musculoskeletal pain:
Bone, joint, and/or muscle pain has been reported in patients taking bisphosphonates. In post-marketing experience, these symptoms have sometimes 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 re-challenged with the same medicine or another bisphosphonate.

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 three 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 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 and receive appropriate orthopaedic care. Poor healing of these fractures has also been reported. Bisphosphonate treatment should be stopped in patients with stress fractures and they should receive appropriate orthopaedic care.

During OSTEONATE PLUS ONCE A WEEK 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.

Bone and mineral metabolism:
Causes of osteoporosis other than oestrogen deficiency and aging should be considered. Hypocalcaemia must be corrected before initiating therapy with OSTEONATE PLUS ONCE A WEEK (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 OSTEONATE PLUS ONCE A WEEK.

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) (see section 4.8).

Cholecalciferol
Vitamin D_3 may increase the magnitude of hypercalcaemia and/or hypercalciuria when administered to patients with diseases associated with unregulated overproduction of calcitriol (e.g. leukaemia, lymphoma, sarcoidosis). Urine and serum calcium should be monitored in these patients.

Patients with malabsorption may not adequately absorb vitamin D_3.

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.

Use in the elderly:
In clinical studies, there was no age-related difference in the efficacy or safety profiles of alendronic acid or cholecalciferol, as contained in OSTEONATE PLUS ONCE A WEEK.

Sugar:
OSTEONATE PLUS ONCE A WEEK contains lactose.
Patients with the rare hereditary conditions of galactose intolerance e.g. galactosaemia, Lapp lactase deficiency or glucose-galactose malabsorption should not take OSTEONATE PLUS ONCE A WEEK. OSTEONATE PLUS ONCE A WEEK contains sucrose. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

4.5 Interaction with other medicines and other forms of interaction
Alendronic acid
It is likely that food and beverages (including mineral water) (see section 4.2), calcium supplements, antacids and other oral medicines, if taken concomitantly, will interfere with absorption of alendronate. Therefore, patients must wait at least 30 minutes after taking OSTEONATE PLUS ONCE A WEEK before taking any other oral medicine. No other interactions of clinical significance are anticipated.

A small number of post-menopausal women in the osteoporosis trials received oestrogen (intravaginal, transdermal or oral) while taking OSTEONATE PLUS ONCE A WEEK. No adverse experiences attributable to their concomitant use were identified.

Specific interaction studies were not performed. In post-menopausal osteoporosis studies, alendronate, an ingredient of OSTEONATE PLUS ONCE A WEEK, was used with a wide range of commonly prescribed medicines without evidence of clinical adverse interactions.
Since nonsteriodal anti-inflammatory medicine (NSAID) use is associated with gastrointestinal irritation, caution should be used during concomitant use with alendronate.

Cholecalciferol
Olestra, mineral oils, orlistat and bile acid sequestrants (e.g. cholestyramine, colestipol) may impair the absorption of vitamin D.
Anticonvulsants, cimetidine and thiazides may increase the catabolism of vitamin D.
Additional vitamin D supplements may be considered on an individual basis.

4.6 Fertility, pregnancy and lactation
Pregnancy
OSTEONATE PLUS ONCE A WEEK has not been studied in pregnant women and is therefore contraindicated (see section 4.3). Studies in animals have shown reproductive toxicity.

Breastfeeding
OSTEONATE PLUS ONCE A WEEK is contraindicated in breastfeeding women as safety and efficacy have not been established (see section 4.3).

Fertility
There is 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
Certain adverse reactions that have been reported with OSTEONATE PLUS ONCE A WEEK may affect patients' ability to drive or operate machinery e.g. blurred vision, dizziness and severe bone muscle or joint pain (see section 4.8). Patients should be warned not to drive or use machines until they know how this medicine affect them.

4.8 Undesirable effects
a). Summary of the safety profile
The most commonly reported adverse reactions are upper gastrointestinal adverse reactions including abdominal pain, dyspepsia, oesophageal ulcer, dysphagia, abdominal distension and acid regurgitation (>1 %).

b). Tabulated summary of adverse reactions

System Organ Class	Frequency	Side effects
Immune system disorders	*Less frequent*	Hypersensitivity reactions including urticaria and angioedema*
Metabolism and nutrition disorders	*Less frequent*	Symptomatic hypocalcaemia, generally in association with predisposing conditions*
Nervous system disorders	*Frequent*	Headache, dizziness*
	Less frequent	Dysgeusia*
Eye disorders	*Less frequent*	Eye inflammation (Uveitis*, scleritis*, episcleritis*)
Ear and labyrinth disorders	*Frequent*	Vertigo*
	Less frequent	Osteonecrosis of the external auditory canal (bisphosphonate class adverse reaction)
Gastrointestinal disorders	*Frequent*	Abdominal pain, dyspepsia, constipation, diarrhoea, flatulence, oesophageal ulcer*, dysphagia*, abdominal distension, acid regurgitation
	Less frequent	Nausea, vomiting*, gastritis, oesophagitis*, oesophageal erosions*, melaena, oesophageal stricture*, oropharyngeal ulceration, gastric or duodenal ulcers, some severe and with complications, upper gastrointestinal PUBs (perforation, ulcers, bleeding)
	Frequency unknown	Oesophageal perforations* (see section 4.4)
Skin and subcutaneous tissue disorders	*Frequent*	Alopecia, pruritus
	Less frequent	Rash, erythema, rash with photosensitivity*, severe skin reactions* including Stevens-Johnson syndrome* and toxic epidermal necrolysis*
Musculoskeletal, connective tissue and bone disorders	*Frequent*	Musculoskeletal (bone, muscle or joint) pain which is sometimes severe, joint swelling*
	Less frequent	Localised osteonecrosis of the jaw*, generally associated with tooth extraction and/or local infection, with delayed healing (see section 4.4), atypical subtrochanteric and diaphyseal femoral fractures (bisphosphonate class adverse reaction)
	Frequency unknown	Severe and/or incapacitating bone, joint, and/or muscle pain* (see section 4.4), low-energy femoral shaft fracture*
General disorders and administrative site conditions	*Frequent*	Asthenia*, peripheral oedema*
	Frequency unknown	Transient symptoms as in an acute-phase response* (myalgia*, malaise* and rarely, fever*) have been reported with alendronate, usually in association with initiation of treatment, and typically in association with the initiation of treatment
Investigations	*Frequency unknown*	Asymptomatic, mild and transient decreases in serum calcium and phosphate

*Post marketing adverse reactions.

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 online service for adverse drug reaction reporting by following the link: https://www.sahpra.org.za/Publications/Index/8.
An email can be sent directly to the company, pharmacovigilance@pharmadynamics.co.za to ensure safety of the product.

4.9 Overdose
Signs and symptoms:
Alendronic acid
Hypocalcaemia, hypophosphataemia and upper gastro-intestinal side effects, such as upset stomach, heartburn, oesophagitis, gastritis or ulcer, may result from oral overdosage.

Cholecalciferol
Vitamin D toxicity may occur with hypercalcaemia or hypercalciuria. This has not been documented during chronic therapy in generally healthy adults at a dose < 10 000 IU/day. In a clinical study of healthy adults, a 4000 IU daily dose of vitamin D_3 for up to five months was not associated with hypercalciuria or hypercalcaemia.

Management of overdose:
Alendronic acid
No specific information is available on the treatment of overdosage with alendronate, as contained in OSTEONATE PLUS ONCE A WEEK.
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.

Cholecalciferol
Treatment is supportive and symptomatic.

5. PHARMACOLOGICAL PROPERTIES
5.1 Pharmacodynamic properties
Pharmacotherapeutic group: Drugs for treatment of bone diseases, Bisphosphonates, combinations
ATC code: M05BB03
Pharmacological classification: A.3.2 Connective tissue medicines, non-hormonal preparations

Mechanism of action
Alendronic acid
Alendronic acid, a bisphosphonate, acts as a specific inhibitor of osteoclast-mediated bone resorption. Bisphosphonates are synthetic analogues of pyrophosphate that bind to the hydroxyapatite found in bone.

Cholecalciferol
Cholecalciferol (vitamin D_3) is a secosterol; the natural precursor of the calcium-regulating hormone calcitriol (1,25-dihydroxyvitamin D_3).
Vitamin D_3 is converted to 25-hydroxyvitamin D_3 in the liver. Conversion to the active calcium-mobilising hormone 1,25-dihydroxyvitamin D_3 (calcitriol) occurs in the kidney. The principal action of 1,25-dihydroxyvitamin D_3 is to increase intestinal absorption of both calcium and phosphate as well as regulate serum calcium, renal calcium and phosphate excretion, bone formation and bone resorption.

5.2 Pharmacokinetic properties
Absorption:
Alendronic acid
The mean oral bioavailability of alendronate in women is 0,57 % for the 70 mg tablet when administered after an overnight fast, and 2 hours before a standardised breakfast. The alendronate in the alendronate/cholecalciferol tablet and an alendronic acid 70 mg tablet show similar bioavailability.

Bioavailability is decreased similarly (by approximately 40 %) whether alendronate is administered 1 hour or ½ hour prior to a standardised breakfast. Alendronate is effective when administered at least ½ hour before the first food or beverage of the day (see section 4.2). Bioavailability is negligible whether alendronate is administered with or up to two hours after a standardised breakfast. Concomitant administration of alendronate with coffee or orange juice reduces bioavailability by approximately 60 %.

Cholecalciferol
Following administration of an alendronate/cholecalciferol 70 mg/2800 IU tablet after an overnight fast and 2 hours before a standard meal, the mean area under the serum-concentration-time curve ($AUC_{0\text{-}120\ hrs}$) for vitamin D_3 was 296,4 ng-hr/mL. The mean maximal serum concentration (C_{max}) of vitamin D_3 is 5,9 ng/mL, and the median time to maximal serum concentration (T_{max}) was 12 hours. The bioavailability of the 2800 IU vitamin D_3 from an alendronate/cholecalciferol tablet is similar to 2800 IU vitamin D_3 administered alone.

Following administration of the 70 mg alendronate/5600 IU cholecalciferol tablet after an overnight fast and 2 hours before a meal, the mean area under the serum-concentration-time curve ($AUC_{0\text{-}80h}$) for vitamin D_3 was 490,2 ng-hr/mL. The mean maximal serum concentration (C_{max}) of vitamin D_3 was 12,2 ng/mL, and the median time to maximal serum concentration (T_{max}) was 10,6 hours. The bioavailability of the vitamin D_3 in 70 mg alendronate/5600 IU cholecalciferol tablet is similar to an equal dose vitamin D_3 administered alone.

Distribution:
Alendronic acid
Studies in rats show that alendronate transiently distributes to soft tissues following 1 mg/kg IV administration but is then rapidly redistributed to bone or excreted in the urine. The mean steady state volume of distribution, exclusive of bone, is at least 28 litres in humans. Concentrations of alendronate in the plasma, following therapeutic oral doses, are too low for analytical detection (less than 5 ng/mL). Protein binding in human plasma is approximately 78 %.

Cholecalciferol
Following absorption, vitamin D_3 enters the blood as part of chylomicrons. Vitamin D_3 is distributed mostly to the liver where it undergoes metabolism to 25-hydroxyvitamin D_3, the major storage form. Lesser amounts are distributed to adipose and muscle tissue and stored as vitamin D_3 at these sites for later release into the circulation. Circulating vitamin D_3 is bound to vitamin D-binding protein.

Biotransformation:
Alendronic acid
There is no evidence that alendronate is metabolised in animals or humans.

Cholecalciferol
Vitamin D_3 is metabolised by hydroxylation in the liver to 25-hydroxyvitamin D_3, and subsequently metabolised in the kidney to the biologically active form - 1,25-dihydroxyvitamin D_3. Further hydroxylation occurs prior to elimination. A small percentage of vitamin D_3 undergoes glucuronidation prior to elimination.

Elimination:
Alendronic acid
Following a single IV dose of [^{14}C] alendronate, approximately 50 % of the radioactivity was excreted in the urine within 72 hours and little or no radioactivity was recovered in the faeces. Following a single 10 mg IV dose, the renal clearance of alendronate was 71 mL/min. Plasma concentrations fell by more than 95 % within 6 hours following IV administration. The terminal half-life in humans is estimated to exceed 10 years, reflecting release of alendronate from the skeleton.

Cholecalciferol
When radioactive vitamin D_3 was administered to healthy subjects, the mean urinary excretion of radioactivity after 48 hours was 2,4 %, and the mean faecal excretion of radioactivity after 4 days was 4,9 %. In both cases, the excreted radioactivity is almost exclusively as metabolites of the parent compound. The mean half-life of vitamin D_3 in the serum following an oral dose of the 70 mg alendronate, 2800 IU cholecalciferol tablet is approximately 24 hours.

Pharmacokinetics in special patient groups
Renal impairment
Preclinical studies show that alendronate that is not deposited in bone is rapidly excreted in the urine. No evidence of saturation of bone uptake was found after chronic dosing with cumulative intravenous doses up to 35 mg/kg in animals. 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 also sections 4.2 and 4.3).

6. PHARMACEUTICAL PARTICULARS
6.1 List of excipients
Aluminium magnesium silicate
Butylhydroxytoluene (BHT) E321
Croscarmellose sodium
Gelatin (100 Bloom)
Lactose
Magnesium stearate
Maize Starch
Microcrystalline cellulose
Sunflower oil (refined)
Sucrose

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
2 years.

6.4 Special precautions for storage
Store at or below 25 °C.
Store in the original blister in order to protect from moisture and light.

6.5 Nature and contents of container
OSTEONATE PLUS ONCE A WEEK tablets are packed in PA/ALL/PVC - aluminium foil (Alu–Alu) blister strips, inside a carton. Each carton contains 4 tablets.

6.6 Special precautions for disposal
No special requirements.

7. HOLDER OF THE CERTIFICATE OF REGISTRATION
Pharma Dynamics (Pty) Ltd
1st Floor Grapevine House, Steenberg Office Park
Silverwood Close
Westlake, Cape Town
7945, South Africa

8. REGISTRATION NUMBER(S)
OSTEONATE PLUS 2800 ONCE A WEEK: A50/3.2/0636
OSTEONATE PLUS 5600 ONCE A WEEK: A50/3.2/0637

9. DATE OF FIRST AUTHORISATION
June 2022

PATIENT INFORMATION LEAFLET

SCHEDULING STATUS S3

OSTEONATE PLUS 2800 ONCE A WEEK tablets.
70 mg alendronic acid and 70 mcg cholecalciferol (2800 IU vitamin D_3)
OSTEONATE PLUS 5600 ONCE A WEEK tablets.
70 mg alendronic acid and 140 mcg cholecalciferol (5600 IU vitamin D_3)

OSTEONATE PLUS ONCE A WEEK contains sugar (lactose and sucrose) in the following quantities, respectively:
OSTEONATE PLUS 2800 ONCE A WEEK: 87,140 mg; 13,745 mg
OSTEONATE PLUS 5600 ONCE A WEEK: 59,140 mg; 27,490 mg

Read all of this leaflet carefully before you start taking OSTEONATE PLUS ONCE A WEEK
- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other healthcare provider.
- OSTEONATE PLUS ONCE A WEEK has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

What is in this leaflet

1. What OSTEONATE PLUS ONCE A WEEK is and what it is used for
2. What you need to know before you use OSTEONATE PLUS ONCE A WEEK
3. How to take OSTEONATE PLUS ONCE A WEEK
4. Possible side effects
5. How to store OSTEONATE PLUS ONCE A WEEK
6. Contents of the pack and other information

1. What OSTEONATE PLUS ONCE A WEEK is and what it is used for
OSTEONATE PLUS ONCE A WEEK is a tablet containing the two active substances, alendronic acid (commonly called alendronate) and cholecalciferol known as vitamin D_3.

Alendronate belongs to a group of non-hormonal medicines called bisphosphonates. Alendronate prevents the loss of bone that occurs in women after they have been through menopause and helps to rebuild bone. It reduces the risk of spine and hip fractures.

Vitamin D is an essential nutrient, required for calcium absorption and healthy bones.
The body can only absorb calcium properly from our food if it has enough vitamin D. Very few foods contain vitamin D. The main source is through exposure to summer sunlight, which makes vitamin D in our skin. As we get older our skin makes less vitamin D. Too little vitamin D may lead to bone loss and osteoporosis. Severe vitamin D deficiency may cause muscle weakness which can lead to falls and a greater risk of fractures.

OSTEONATE PLUS ONCE A WEEK is used to treat your osteoporosis (a thinning and weakening of the bones). OSTEONATE PLUS ONCE A WEEK may reduce your risk of developing bone fractures, including those of the hip and spine and to help ensure vitamin D adequacy.

2. What you need to know before you take OSTEONATE PLUS ONCE A WEEK
Do not take OSTEONATE PLUS ONCE A WEEK:
- if you are hypersensitive (allergic) to alendronate, cholecalciferol, or to any of the ingredients of OSTEONATE PLUS ONCE A WEEK (see section 6)
- if you have certain problems with your oesophagus (the tube that connects your mouth to your stomach), such as narrowing or difficulty swallowing
- if you are unable to stand or sit upright for at least 30 minutes
- if your doctor has told you that you have low calcium levels in your blood
- if you have severe kidney problems
- if you are pregnant or breastfeeding your baby
- children under 18 years of age.

Warnings and precautions
Tell your doctor before taking OSTEONATE PLUS ONCE A WEEK if:
- you have any upper gastro-intestinal problems, such as difficulty or pain when swallowing, diseases of the tube connecting your throat to your stomach (oesophagus) (including Barrett's oesophagus, where the lower portion of your oesophagus is damaged from repeated exposure to stomach acid), inflammation of your stomach lining (gastritis), inflammation of the first part of your small intestine (duodenitis), or ulcers, or if you have had a stomach ulcer within the previous year, active gastrointestinal bleeding, or surgery of your upper gastrointestinal tract.

These conditions may worsen if you continue to take OSTEONATE PLUS ONCE A WEEK after developing these symptoms:
- you are taking a nonsteroidal anti-inflammatory medicine (NSAID) for rheumatism or long-term pain. Both medicines can cause irritation to the lining of the stomach and intestine
- you have low blood levels of calcium (hypocalcaemia), vitamin D, or parathyroid hormone (hypoparathyroidism). Your doctor may need to monitor your blood levels closely
- you have cancer. This may increase your risk of developing damage in the jaw (osteonecrosis) generally associated with delayed healing and infection
- you have blood cancer (leukaemia), cancer of the body's disease-fighting network (lymphoma) or a disease that causes the growth of inflammatory cell collections most often in the lungs and lymph nodes (sarcoidosis). Your doctor may need to monitor your blood levels closely
- you suffer from having trouble absorbing minerals in your stomach or intestines (malabsorption syndrome). Vitamin D_3 absorption may be impacted
- you are undergoing chemotherapy, radiotherapy or you are taking a medicine that blocks blood flow to and growth of cancer cells (angiogenesis inhibitors) or taking any steroid medicine. This may increase your risk of developing jaw osteonecrosis
- you have poor dental health, gum disease, other dental disease, poorly fitting dentures, you have a planned tooth extraction or other invasive dental procedure, or you do not receive routine dental care. This may increase your risk of developing jaw osteonecrosis
- you have a condition that reduces blood and oxygen flow to organs of the body (anaemia), have a condition that causes excessive bleeding or excessive clotting (coagulopathy), have an infection or you are or have been a smoker. This may increase your risk of dental problems and developing jaw osteonecrosis.

You may be advised to have a dental check-up before starting treatment with OSTEONATE PLUS ONCE A WEEK.

It is important to maintain good oral hygiene when being treated with OSTEONATE PLUS ONCE A WEEK. You should have routine dental check-ups throughout your treatment, and you should contact your doctor or dentist if you experience any problems with your mouth or teeth such as loose teeth, pain or swelling.

If you get any of these symptoms or diseases, during your treatment with OSTEONATE PLUS ONCE A WEEK, tell your doctor straight away because it could be serious:
- difficulty or pain when swallowing, chest pain or new or worsening heartburn. These symptoms are more likely to occur if you lie down within 30 minutes after taking OSTEONATE PLUS ONCE A WEEK and/or you do not swallow the tablets with a full glass of water. These symptoms can become severe and could lead to hospitalisation. Discontinue OSTEONATE PLUS ONCE A WEEK and contact your doctor
- you experience bone, joint or muscle pain
- you experience pain, swelling, tenderness and/or bruising in your thigh, hip or groin. This could be an indication of stress fractures in your leg bone. Your doctor will indicate the correct treatment for this
- you experience ear problems such as pain, discharge or ear infection.

Other medicines and OSTEONATE PLUS ONCE A WEEK
Always tell your healthcare provider if you are taking any other medicine. (This includes complementary or traditional medicines.)

It is likely that calcium supplements, antacids and some oral medicines may interfere with the absorption of alendronate, if taken at the same time as OSTEONATE PLUS ONCE A WEEK. It is therefore important that you wait at least 30 minutes after taking OSTEONATE PLUS ONCE A WEEK before taking any of these other oral medicines or supplements.

Certain medicines for rheumatism or long-term pain, called nonsteroidal anti-inflamatory medicine (NSAIDs) (e.g. aspirin and ibuprofen) may cause digestive problems.

Caution should be used when taking these medicines with OSTEONATE PLUS ONCE A WEEK.

It is likely that some food additives or medicines (including artificial fat substitutes, mineral oils, the weight loss medicine orlistat, and the cholesterol-lowering medicines cholestyramine and colestipol) may prevent the vitamin D, as contained in OSTEONATE PLUS ONCE A WEEK from being absorbed into your body.

Medicines used to treat seizures, cimetidine used as treatment for stomach ulcers, and thiazides (water tablets) used to lower blood pressure, may decrease the effectiveness of vitamin D. Your doctor may advise you to take additional vitamin D supplements if you are taking any of these medicines with OSTEONATE PLUS ONCE A WEEK.

OSTEONATE PLUS ONCE A WEEK with food and drink
It is likely that food and drinks (including bottled mineral water), taken at the same time as OSTEONATE PLUS ONCE A WEEK, will decrease the absorption of alendronate and reduce the effectiveness of OSTEONATE PLUS ONCE A WEEK. It is therefore important that you wait at least 30 minutes after taking OSTEONATE PLUS ONCE A WEEK before you eat or drink anything (except water).

Pregnancy, breastfeeding and fertility
If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist or other healthcare provider for advice before taking OSTEONATE PLUS ONCE A WEEK.

OSTEONATE PLUS ONCE A WEEK is only intended for use in postmenopausal women.
Do not take OSTEONATE PLUS ONCE A WEEK if you are pregnant or breastfeeding your baby.

Driving and using machines
OSTEONATE PLUS ONCE A WEEK may cause side effects such as blurred vision, dizziness and severe bone muscle or joint pain, which could affect your ability to drive and use machines.
It is not always possible to predict to what extent OSTEONATE PLUS ONCE A WEEK may interfere with the daily activities of a patient. Patients should ensure that they do not engage in the above activities until they are aware of the measure to which OSTEONATE PLUS ONCE A WEEK affects them.

OSTEONATE PLUS ONCE A WEEK contains lactose and sucrose
OSTEONATE PLUS ONCE A WEEK contains lactose and sucrose. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

3. How to take OSTEONATE PLUS ONCE A WEEK
Do not share medicines prescribed for you with any other person. Always use OSTEONATE PLUS ONCE A WEEK exactly as described in this leaflet or as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

The usual dose is one tablet of OSTEONATE PLUS ONCE A WEEK taken once a week.

Follow these instructions carefully to ensure you benefit from OSTEONATE PLUS ONCE A WEEK:
- choose a day of the week to take your tablet. Every week, take one OSTEONATE PLUS ONCE A WEEK tablet on that day
- to help OSTEONATE PLUS ONCE A WEEK reach your stomach quickly and to reduce the chance of irritation when swallowing, OSTEONATE PLUS ONCE A WEEK must be taken at least 30 minutes before the first food, drink or other medication of the day
- OSTEONATE PLUS ONCE A WEEK should be swallowed with a full glass of water only. Do not take OSTEONATE PLUS ONCE A WEEK with bottled water, tea, coffee, milk or juice
- swallow the tablet whole. Do not crush, chew or suck the tablet
- you should not lie down for at least 30 minutes after taking OSTEONATE PLUS ONCE A WEEK, and do not lie down until you have eaten
- do not take OSTEONATE PLUS ONCE A WEEK at bedtime or before getting up in the morning
- if you develop difficulty or pain in swallowing, chest pain, or new or worsening heartburn, stop taking OSTEONATE PLUS ONCE A WEEK and contact your doctor.

Your doctor may tell you to take calcium and/or vitamin D supplements whilst you are taking OSTEONATE PLUS ONCE A WEEK.

Children:
Children under 18 years of age should not take OSTEONATE PLUS ONCE A WEEK (see Do not take OSTEONATE PLUS ONCE A WEEK).

Your doctor will tell you how long your treatment with OSTEONATE PLUS ONCE A WEEK will last. Do not stop treatment early because your symptoms may return.
If you have the impression that the effect of OSTEONATE PLUS ONCE A WEEK is too strong or too weak, tell your doctor or pharmacist.

If you take more OSTEONATE PLUS ONCE A WEEK than you should
In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison control centre.

If you take too many tablets by mistake, drink a full glass of milk and contact your doctor immediately. Do not make yourself vomit, and do not lie down.

Symptoms of overdose may include:
- reduced levels of calcium and phosphates in your blood, upset stomach, heartburn, inflammation of the oesophagus, stomach pain with nausea or vomiting, ulcer.

If you forget to take OSTEONATE PLUS ONCE A WEEK
If you forget to take OSTEONATE PLUS ONCE A WEEK, take in the morning after you remember. Return to taking one tablet once a week on the original chosen day. Do not take a double dose to make up for forgotten individual doses.

If you stop taking OSTEONATE PLUS ONCE A WEEK
It is important that you take OSTEONATE PLUS ONCE A WEEK for as long as your doctor prescribes the medicine. Since it is not known how long you should take OSTEONATE PLUS ONCE A WEEK, you should discuss the need to stay on this medicine with your doctor periodically to determine if OSTEONATE PLUS ONCE A WEEK is still right for you.

4. Possible side effects
OSTEONATE PLUS ONCE A WEEK can have side effects.
Not all side effects reported for OSTEONATE PLUS ONCE A WEEK are included in this leaflet. Should your general health worsen, or if you experience any untoward effects while using OSTEONATE PLUS ONCE A WEEK, please consult your healthcare provider for advice.

If any of the following happens, stop using OSTEONATE PLUS ONCE A WEEK and tell your doctor immediately or go to the casualty department at your nearest hospital:
- swelling of the hands, feet, ankles, face, lips, mouth or throat, which may cause difficulty in swallowing or breathing
- rash or itching
- fainting.

These are all very serious side effects. If you have them, you may have had a serious reaction to OSTEONATE PLUS ONCE A WEEK. You may need urgent medical attention or hospitalisation.

Tell your doctor immediately or go to the casualty department at your nearest hospital if you notice any of the following:
- irritation or ulceration of the oesophagus, difficulty or pain when swallowing, chest pain or worsening heartburn. These reactions are more likely to occur if you lie down within 30 minutes after taking OSTEONATE PLUS ONCE A WEEK and/or you do not swallow the tablets with a full glass of water
- Stevens-Johnson syndrome (begins with flu-like symptoms, followed by a painful red or purplish rash that spreads and blisters), toxic epidermal necrolysis (TEN) (a life-threatening skin disorder with symptoms such as a painful red area that spreads quickly, skin peeling without blisters, raw areas of skin) or other serious skin disorders.

These are all serious side effects. You may need urgent medical attention.

Tell your doctor if you notice any of the following:
Frequent side effects:
- headache
- stomach pain, indigestion or belching, constipation, diarrhoea, flatulence, sore throat with ulcers, difficulty or discomfort in swallowing (dysphagia), full or bloated stomach, acid reflux
- bone, muscle or joint pain
- dizziness, feeling dizzy when standing still (vertigo)
- pruritus (itching)
- hair loss (alopecia).

Less frequent side effects:
- irritation or inflammation of the gullet (oesophagus – the tube that connects your mouth with your stomach) or stomach, heartburn, ulcer (painful sore) located in the lining of the lower part of the oesophagus, swelling of the throat, hole in the oesophagus, stomach or peptic ulcers (sometimes severe or with bleeding)
- nausea, vomiting, black and/or tar-like stools
- severe bone joint or muscle pain that hinders movement, joint swelling, unusual fracture of the thigh bone
- pain in the mouth and/or jaw, swelling or sores inside the mouth, numbness or a feeling of heaviness in the jaw, or loosening of a tooth. These could be signs of bone damage in the jaw (osteonecrosis) generally associated with delayed healing and infection, often following tooth extraction
- inflammation, pain or redness of the eye, blurred vision or loss of vision
- temporary flu-like symptoms, such as aching muscles, generally feeling unwell and weak; sometimes with fever, usually at the start of treatment, swelling of the legs or ankles
- rash, superficial reddening of the skin, usually in patches
- severe itching of the skin (pruritis), skin rash, sensitivity to sunlight
- changes in mineral levels in the blood
- decreased taste sensitivity
- symptoms of low blood calcium levels including muscle cramps or spasms and/or tingling sensation in the fingers or around the mouth
- ear pain, discharge from the ear, and/or an ear infection. These could be signs of bone damage in the ear.

The following side effects have been reported but the frequency for them to occur is not known:
- severe bone, joint or muscle pain that hinders movement, joint swelling
- unusual thighbone fracture
- brief occurrence of muscle pain and fever
- laboratory test results indicating decreased calcium and phosphate in the blood.

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

Reporting of side effects
If you get side effects, talk to your doctor, pharmacist or nurse. You can also report any side effects to SAHPRA via the online service for adverse drug reaction reporting by following the link:
https://www.sahpra.org.za/Publications/Index/8
By reporting side effects, you can help provide more information on the safety of OSTEONATE PLUS ONCE A WEEK. You can also send an email directly to the company, pharmacovigilance@pharmadynamics.co.za to ensure safety of the product.

5. How to store OSTEONATE PLUS ONCE A WEEK
Store all medicines out of reach of children.
Store at or below 25 °C.
Store in the original blister in order to protect from moisture and light.
Do not use after the expiry date stated on the carton. Return all unused medicine to your pharmacist.
Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

6. Contents of the pack and other information
What OSTEONATE PLUS ONCE A WEEK contains
OSTEONATE PLUS 2800 ONCE A WEEK: The active ingredients are sodium alendronate trihydrate equivalent to 70 mg alendronic acid and cholecalciferol concentrate (powder form) equivalent to 70 mcg cholecalciferol (2800 IU Vitamin D_3).

OSTEONATE PLUS 5600 ONCE A WEEK: The active ingredients are sodium alendronate trihydrate equivalent to 70 mg alendronic acid and cholecalciferol concentrate (powder form) equivalent to 140 mcg cholecalciferol (5600 IU Vitamin D_3).

The other ingredients are:
Aluminium magnesium silicate, butylhydroxytoluene (BHT) E321, croscarmellose sodium, gelatin (100 Bloom), lactose, magnesium stearate, maize starch, microcrystalline cellulose, sunflower oil (refined) and sucrose.

What OSTEONATE PLUS ONCE A WEEK looks like and contents of the pack
OSTEONATE PLUS 2800 ONCE A WEEK: White to off-white oblong, biconvex tablets, mottled, engraved with 2800 on one side with dimensions 12,3 mm ± 0,2 mm in length and 6,5 ± 0,2 mm in width.

OSTEONATE PLUS 5600 ONCE A WEEK: White to off-white , modified rectangle-shaped tablets, mottled, engraved with 5600 on one side with dimensions 11,4 mm ± 0,2 mm in length and 7,2 ± 0,2 mm in width.

OSTEONATE PLUS ONCE A WEEK tablets are packed in PA/ALL/PVC - aluminium foil (Alu–Alu) blister strips, inside a carton. Each carton contains 4 tablets.

Holder of Certificate of Registration
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Registration number
OSTEONATE PLUS 2800 ONCE A WEEK: A50/3.2/0636
OSTEONATE PLUS 5600 ONCE A WEEK: A50/3.2/0637

PASIËNTINLIGTINGSBLAD

SKEDULERINGSTATUS S3

OSTEONATE PLUS 2800 ONCE A WEEK tablette.
70 mg alendroniese suur en 70 mkg cholekalsiferol (2800 IU vitamien D_3)
OSTEONATE PLUS 5600 ONCE A WEEK tablette.
70 mg alendroniese suur en 140 mkg cholekalsiferol (5600 IU vitamien D_3)

OSTEONATE PLUS ONCE A WEEK bevat suiker (laktose en sukrose) in volgende hoeveelhede, onderskeidelik:
OSTEONATE PLUS 2800 ONCE A WEEK: 87,140 mg; 13,745 mg
OSTEONATE PLUS 5600 ONCE A WEEK: 59,140 mg; 27,490 mg

Lees hierdie hele inligtingsblad deeglik deur, voordat u begin om OSTEONATE PLUS ONCE A WEEK te neem
- Hou hierdie inligtingsblad. Dit mag nodig wees vir u om dit weer lees.
- Indien u verdere vrae het, vra asseblief u dokter, apteker, verpleegkundige, of ander gesondheidsorgverskaffer.
- OSTEONATE PLUS ONCE A WEEK is vir u persoonlik voorgeskryf en u moet nie u medisyne met ander mense deel nie. Dit mag skadelik wees vir hulle, selfs al is hulle simptome dieselfde as u eie.

Wat hierdie inligtingsblad bevat

1. Wat OSTEONATE PLUS ONCE A WEEK is en waarvoor dit gebruik word
2. Wat u nodig het om te weet, voordat u OSTEONATE PLUS ONCE A WEEK gebruik
3. Hoe om OSTEONATE PLUS ONCE A WEEK te neem
4. Moontlike newe-effekte
5. Hoe om OSTEONATE PLUS ONCE A WEEK te bewaar
6. Verpakkingsinhoud en ander inligting

1. Wat OSTEONATE PLUS ONCE A WEEK is en waarvoor dit gebruik word
OSTEONATE PLUS ONCE A WEEK is 'n tablet, wat twee aktiewe bestanddele bevat; alendroniese suur (algemeen bekend as alendronaat) en cholekalsiferol (ook bekend as vitamien D_3).

Alendronaat behoort aan 'n groep nie-hormonale medisyne, wat bisfosfonate genoem word. Alendronaat verhoed die verlies van been wat by vroue voorkom, nadat hulle deur die menopouse-fase gegaan het en help met die herbou daarvan. Dit verminder die risiko vir ruggraat- en heupfrakture.

Vitamien D is 'n noodsaaklike voedingstof, wat benodig word vir kalsiumabsorpsie en gesonde bene. Die liggaam kan slegs kalsium behoorlik vanuit u voedsel absorbeer, indien dit genoeg vitamien D bevat. Baie min voedselgroepe bevat vitamien D. Die hoofbron is deur blootstelling aan somersonlig, wat vitamien D in u vel vervaardig. Soos ons ouer word, vervaardig die vel minder vitamien D. Te min vitamien D, mag lei tot beenverlies en osteoporose. Erge vitamien D tekort, mag spierswakheid veroorsaak, wat kan lei tot valle en 'n groter risiko vir frakture.

OSTEONATE PLUS ONCE A WEEK word aangedui om u osteoporose (verdunning en verswakking van die bene), te behandel. OSTEONATE PLUS ONCE A WEEK mag u risiko vir die ontwikkeling van beenfrakture, insluitend dié van die heup en ruggraat, verlaag en help om genoegsame vitamien D te verseker.

2. Wat u nodig het om te weet, voordat u OSTEONATE PLUS ONCE A WEEK neem
Moet nie OSTEONATE PLUS ONCE A WEEK neem:
- indien u hipersensitief (allergies) is vir alendroniese suur, cholekalsiferol, of vir enige van die ander bestanddele van OSTEONATE PLUS ONCE A WEEK nie (kyk afdeling 6)
- indien u sekere probleme met u slukderm (die buis wat u mond, met u maag verbind), soos vernouing, of probleme met sluk, ondervind nie
- indien u nie in staat is om regop te staan, of te sit, vir ten minste 30 minute, nie
- indien u dokter u ingelig het, dat u lae kalsiumvlakke in u bloed het nie
- indien u erge nierprobleme het nie
- indien u swanger is, of u baba borsvoed nie
- deur kinders jonger as 18 jaar oud nie.

Waarskuwings en voorsorgmaatreëls
Vertel u dokter voordat u OSTEONATE PLUS ONCE A WEEK neem indien:
- u enige boonste gastrointestinale probleme, soos moeilike, of pynlike sluk ervaar, u aan siektes van die buis wat u keel en maag verbind (esofagus) (insluitend Barrett se esofagus, waar die onderste gedeelte van u esofagus beskadig is, weens herhaalde blootstelling aan maagsuur) ly, inflammasie van u maagwand (gastritis) het, u inflammasie van die eerste gedeelte van u dunderm (duodenitis) het, of ulkusse, of indien u 'n maagseer tydens die vorige jaar gehad het, u aan gastrointestinale bloeding ly, of 'n operasie van u boonste gastrointestinale kanaal gehad het.

Hierdie toestande mag vererger indien u aanhou om OSTEONATE PLUS ONCE A WEEK te gebruik, nadat hierdie simptome ontwikkel het
- u niesteroïdale anti-inflammatoriese medisyne (NSAIM) vir rumatiek of langtermyn pyn neem. Beide medisyne mag irritasie van die maagwand en derms, veroorsaak
- u lae kalsiumbloedvlakke (hipokalsemie), vitamien D, of paratiroïedhormoon (hipoparatiroïedisme) het. Dit mag nodig wees vir u dokter om u bloedvlakke noukeurig te monitor
- u kanker het. Dit mag u risiko vir die ontwikkeling van skade aan u kakebeen (osteonekrose), algemeen geassosieer met 'n vetraging in genesing en infeksie
- u bloedkanker het (leukemie), kanker van die liggaam se immuun-vegtende netwerk (limfoom), of 'n siekte wat die groei van inflammatoriese selgroepe (meer dikwels in die longe en limfnode (sarkoïdose)). Dit mag nodig wees vir u dokter om u bloedvlakke noukeurig te monitor
- u dit moeilik vind om minerale in u maag of derms te absorbeer (wanabsorpsie-sindroom). Vitamien D_3 absorbsie mag beinvloed word
- u chemoterapie of radioterapie ondergaan, of u 'n medisyne neem wat die bloedvloei na, en die groei van kankerselle vertraag (angiogenese inhibitors), of indien u steroiedmedisyne neem. Dit mag u risiko vir die ontwikkeling van kakebeen-osteonekrose, verhoog
- u swak tandhigiëne, tandvleissiekte, of ander tandsiekte, swak-passende valstande het, u 'n tandonttrekking of ander ingrypende tandheelkundige prosedure beplan, of u nie gereelde tandheelkundige sorg ontvang nie. Dit mag u risiko vir die ontwikkeling van kakebeen-osteonekrose, verhoog
- u 'n toestand ervaar waar die bloedvloei en suurstof na liggaamsorgane verminder (anemie), u aan 'n toestand ly wat uitermatige bloeding, of bloedstolling veroorsaak (koagulopatie), u 'n infeksie het of 'n roker was. Dit mag u risiko vir tandheelkindige probleme en die ontwikkeling van kakebeen osteonekrose, verhoog.

U mag aangeraai word om 'n tandheelkundige ondersoek te ondergaan, voordat u met OSTEONATE PLUS ONCE A WEEK begin.

Dit is belangrik om goeie mondhigiëne te handhaaf, terwyl u met OSTEONATE PLUS ONCE A WEEK behandel word. U moet roetine tandheelkundige ondersoeke deurgaans u behandeling ondergaan en u moet u dokter, of tandarts raadpleeg, indien u enige probleme met u mond, of tande, soos los tande, pyn, of swelling ervaar.

Indien u enige van hierdie simptome, of siektes tydens u behandeling met OSTEONATE PLUS ONCE A WEEK ervaar, vertel u dokter onmiddellik, aangesien dit ernstig mag wees:
- sluk moeilik of pynlik, borskaspyn, of verergering van sooibrand. Hierdie simptome kom meer waarskynlik voor, indien u binne 30 minute, nadat u OSTEONATE PLUS ONCE A WEEK geneem het, gaan lê en/of nie die tablette met 'n vol glas water, sluk nie. Hierdie simptome mag vererger en hospitalisasie benodig. Onttrek OSTEONATE PLUS ONCE A WEEK en raadpleeg u dokter
- indien u been-, gewrigs-, of spierpyn ervaar
- indien u pyn, swelling, gevoeligheid en/of kneusing in u dy, heup of lies ervaar. Dit mag 'n indikasie van stresfakture in u dybeen wees. U dokter sal die gepaste behandeling vir hierdie toestand aanbeveel
- indien u oorprobleme, soos pyn, afskeiding, of oorinfeksie ervaar.

Ander medisyne en OSTEONATE PLUS ONCE A WEEK
Vertel altyd u gesondheidsorgverskaffer indien u enige ander medisyne neem (Dit sluit aanvullende, of tradisionele medisyne in).

Dit is heel waarskynlik, dat kalsiumaanvullings, teensuurmiddels en sekere mondelikse medisyne, met die absorpsie van alendronaat mag inmeng, indien dit op dieselfde tydstip as OSTEONATE PLUS ONCE A WEEK geneem word. Dit is dus belangrik dat u vir ten minste 30 minute wag, nadat u OSTEONATE PLUS ONCE A WEEK geneem het, voordat u enige van hierdie orale medisyne, of aanvullings neem.

Sekere medisyne vir rumatiek, of langtermyn pyn, ook niesteroïedale anti-inflammatoriese medisyne (NSAIMs) genoem (bv. aspirien en ibuprofen), mag spysverteringsprobleme veroorsaak.

Omsigtigheid moet uitgeoefen word wanneer hierdie medisyne saam met OSTEONATE PLUS ONCE A WEEK geneem word.

Dit is waarskynlik dat sekere voedingsbymiddels, of medisyne (insluitend kunsmatige vetvervangers, minerale olies, die gewigsverlies medisyne orlistat en die cholesterol-verlagende medisyne cholestiramien en kolestipol), mag verhoed dat vitamien D, soos bevat in OSTEONATE PLUS ONCE A WEEK, in u liggaam geabsorbeer word.

Medisyne wat gebruik word om aanvalle te behandel, simetidien (gebruik as behandeling vir maagsere) en tiasiede (watertablette), wat gebruik word om bloeddruk te verlaag, mag die doeltreffendheid van vitamien D verlaag. U dokter mag aanbeveel dat u bykomende vitamien D aanvullings neem, indien u enige van hierdie medisyne, saam met OSTEONATE PLUS ONCE A WEEK gebruik.

OSTEONATE PLUS ONCE A WEEK saam met kos en drinkgoed
Dit is waarskynlik dat kos en drinkgoed (insluitend gebottelde mineraalwater), wat op dieselfde tydstip as OSTEONATE PLUS ONCE A WEEK geneem word, die absorpsie van alendronaat en die doeltreffendheid van OSTEONATE PLUS ONCE A WEEK sal verlaag. Dit is dus belangrik dat u vir ten minste 30 minute wag, nadat u OSTEONATE PLUS ONCE A WEEK geneem het, voordat u enige iets (behalwe water) eet, of drink.

Swangerskap, borsvoeding en fertiliteit
Indien u swanger is, of borsvoed, vermoed dat u swanger is, of 'n baba beplan, raadpleeg asseblief u dokter, apteker, of ander gesondheidsorgverskaffer vir advies, voordat u OSTEONATE PLUS ONCE A WEEK neem.

OSTEONATE PLUS ONCE A WEEK is slegs bedoel vir gebruik deur post-menopousale vroue.
Moet nie OSTEONATE PLUS ONCE A WEEK neem, indien u swanger is, of u baba borsvoed nie.

Bestuur en die hantering van masjiene
OSTEONATE PLUS ONCE A WEEK mag newe-effekte soos versteurde visie, duiseligheid en erge been-, of gewrigspyn veroorsaak, wat u vermoë om te bestuur en masjiene te hanteer, mag beinvloed.
Dit is nie altyd moontlik om te voorspel tot watter mate OSTEONATE PLUS ONCE A WEEK met die daaglikse aktiwiteite van 'n pasiënt mag inmeng nie. Pasiënte moet verseker dat hulle nie by bogenoemde aktiwiteite betrokke raak, totdat hulle bewus is hoe OSTEONATE PLUS ONCE A WEEK hulle aantas nie.

OSTEONATE PLUS ONCE A WEEK bevat laktose en sukrose
OSTEONATE PLUS ONCE A WEEK bevat laktose en sukrose. Indien u dokter aangedui het, dat u 'n onverdraagsaamheid teenoor sekere suikers toon, raadpleeg u dokter, voordat u hierdie medikasie gebruik.

3. Hoe om OSTEONATE PLUS ONCE A WEEK te neem
Moet nie medisyne wat vir u voorgeskryf is, met enige ander persoon deel nie. Neem OSTEONATE PLUS ONCE A WEEK altyd presies soos in hierdie inligtingsblad beskryf word, of soos deur u dokter aanbeveel word. Raadpleeg u dokter, of apteker, indien u onseker is.

Die gewone dosis is een OSTEONATE PLUS ONCE A WEEK tablet, een keer per week.

Volg hierdie instruksies noukeurig, om te verseker dat u voordeel trek uit die gebruik van OSTEONATE PLUS ONCE A WEEK:
- kies 'n spesifieke dag van die week, om u tablet te neem. Neem een OSTEONATE PLUS ONCE A WEEK tablet elke week, op die vasgestelde dag
- om te verseker dat OSTEONATE PLUS ONCE A WEEK u maag vinnig bereik en om die moontlikheid van irritasie te verminder wanneer u dit insluk, moet OSTEONATE PLUS ONCE A WEEK ten minste 30 minute voor die eerste maaltyd, drinkgoed, of ander medikasie vir die dag, geneem word
- OSTEONATE PLUS ONCE A WEEK moet slegs met 'n vol glas water gesluk word. Moet nie OSTEONATE PLUS ONCE A WEEK met gebottelde water, tee, koffie, melk, of sap, neem nie
- sluk die tablet heel. Moet nie die tablet verbrokkel, kou, of suig nie
- u moet vir ten minste 30 minute nie gaan lê, nadat u OSTEONATE PLUS ONCE A WEEK geneem het nie en moenie lê, voordat u geëet het nie
- moet nie OSTEONATE PLUS ONCE A WEEK teen slapenstyd, of voordat u soggens opstaan, neem nie
- staak die gebruik van OSTEONATE PLUS ONCE A WEEK en raadpleeg u dokter, indien u dit moeilik, of pynlik vind om te sluk, borspyn ervaar, of nuwe sooibrand, of sooibrand wat vererger, ervaar.

U dokter mag aanbeveel dat u kalsium, en/of vitamien D aanvullings neem, terwyl u OSTEONATE PLUS ONCE A WEEK gebruik.

Kinders:
Kinders jonger as 18 jaar oud, moet nie OSTEONATE PLUS ONCE A WEEK neem nie (kyk Moet nie OSTEONATE PLUS ONCE A WEEK neem).

U dokter sal aandui, vir hoe lank u behandeling met OSTEONATE PLUS ONCE A WEEK sal duur. Moet nie behandeling vroegtydig staak nie, aangesien u simptome mag terugkeer.
Indien u onder die indruk is, dat die werking van OSTEONATE PLUS ONCE A WEEK, té sterk, of té swak is, raadpleeg u dokter, of apteker.

Indien u meer OSTEONATE PLUS ONCE A WEEK neem, as wat u behoort
In die geval van oordosering, raadpleeg u dokter, of apteker. Indien beide nie beskikbaar is nie, kontak die naaste hospitaal, of gifbeheersentrum.

Indien u per ongeluk, te veel tablette neem, drink 'n vol glas melk en kontak u dokter onmiddellik. U moet nie probeer om uself te laat braak nie en u moet nie gaan lê nie.

Simptome van oordosering, mag die volgende insluit:
- vermindering in kalsium- en fosfaatvlakke in u bloed, omgekrapte maag, sooibrand, inflammasie van die slukderm, maagpyn met naarheid, of braking, maagseer.

Indien u vergeet om OSTEONATE PLUS ONCE A WEEK te neem
Indien u vergeet om OSTEONATE PLUS ONCE A WEEK te neem, neem dit die volgende oggend. Gaan dan voort om die tablet een keer per week, op die oorspronklike vasgestelde dag te neem. Moet nie 'n dubbel dosis neem, om op te maak vir die vergete, individuele doserings nie.

Indien u die gebruik van OSTEONATE PLUS ONCE A WEEK staak
Dit is belangrik dat u OSTEONATE PLUS ONCE A WEEK neem, vir solank as wat u dokter die medisyne voorgeskryf het. U moet u dokter van tyd tot tyd raadpleeg, om uit te vind of OSTEONATE PLUS ONCE A WEEK nog geskik is vir u, aangesien dit nie bekend is, vir hoe lank u OSTEONATE PLUS ONCE A WEEK, moet neem nie.

4. Moontlike newe-effekte
OSTEONATE PLUS ONCE A WEEK kan newe-effekte hê.
Nie alle newe-effekte wat vir OSTEONATE PLUS ONCE A WEEK aangemeld is, word in hierdie inligtingsblad ingesluit nie. Sou u algemene gesondheid versleg, of indien u enige ongewenste effekte ervaar, terwyl u OSTEONATE PLUS ONCE A WEEK neem, raadpleeg asseblief u gesondheidsorgverskaffer vir advies.

Indien enige van die volgende gebeur, staak die gebruik van OSTEONATE PLUS ONCE A WEEK en vertel u dokter onmiddellik, of gaan na die ongevalle afdeling by u naaste hospitaal:
- swelling van die hande, voete, enkels, gesig, lippe, mond, of keel, wat sluk, of asemhaling, mag bemoeilik
- uitslag, of gejeuk
- floute.

Hierdie is alles baie ernstige newe-effekte. Indien u dit het, kon u 'n ernstige reaksie met OSTEONATE PLUS ONCE A WEEK ervaar het. U mag dringende mediese aandag, of hospitalisasie benodig.

Vertel u dokter onmiddellik, of gaan na die ongevalle afdeling by u naaste hospitaal, indien u enige van die volgende opmerk:
- irritasie, of ulserasie van die slukderm, u vind dit moeilik, of pynlik om te sluk, borspyn, of sooibrand wat vererger. Daar is 'n groter moontlikheid vir hierdie reaksies om voor te kom, indien u gaan lê, binne 30 minute nadat u OSTEONATE PLUS ONCE A WEEK geneem het en/of u nie die tablette, met 'n vol glas water neem nie
- Stevens-Johnson-sindroom (begin met griep-soortige simptome, gevolg deur 'n pynlike, rooi, of perserige uitslag, wat versprei en blasies vorm), toksiese epidermale nekrolise (TEN) ('n lewensbedreigende velversteuring, met simptome soos 'n pynlike rooi oppervlakte, wat vinnig versprei, velafskilfering, sonder blasies, rou velopperviaktes), of ander ernstige velversteurings.

Hierdie is alles ernstige newe-effekte. U mag dringende mediese aandag benodig.

Vertel u dokter, indien u enige van die volgende opmerk:
Newe-effekte wat dikwels voorkom:
- hoofpyn
- maagpyn, ind