APPROVED PROFESSIONAL INFORMATION

SCHEDULING STATUS

S3

PROPRIETARY NAME (and dosage form)

OSSADURA (Tablet)

COMPOSITION

OSSADURA 10 mg:

Each uncoated tablet contains sodium alendronate equivalent to alendronic acid 10 mg.Sugar free.

The other ingredients are cellulose microcrystalline, magnesium stearate, maize starch, povidone and sodium starch glycolate.

OSSADURA 70 mg:

Each uncoated tablet contains sodium alendronate equivalent to alendronic acid 70 mg.Sugar free.

The other ingredients are cellulose microcrystalline, magnesium stearate, maize starch, povidone and sodium starch glycolate.

PHARMACOLOGICAL CLASSIFICATION

A.3.2. Connective tissue medicines, non-hormonal preparations.

PHARMACOLOGICAL ACTION

Bisphosphonates are synthetic analogues of pyrophosphate that bind to the hydroxyapatite found in bone. Alendronate sodium is an aminobisphosphonate that acts as a specific inhibitor of osteoclast–mediated bone resorption.

Alendronate localises preferentially at sites of bone resorption, specifically under osteoclasts, and inhibits osteoclastic bone resorption with no direct effect on bone formation. During exposure to alendronate, normal bone is formed that incorporates alendronate into its matrix where it is pharmacologically inactive.

Pharmacokinetics:

Absorption

The oral bioavailability of alendronate in women is 0,7 % for doses ranging from 5 to 40 mg when administered after an overnight fast and two hours before a standardised breakfast.

The mean oral bioavailability of alendronate in women is 0,57 % for the 70 mg tablet when administered after an overnight fast and two hours before a standardised breakfast.

Oral bioavailability in men (0,6 %) is similar to that in women.

Whether alendronate is administered one or one-half hour before a standardised breakfast, bioavailability is decreased similarly (by approximately 40 %).

In osteoporosis studies, alendronate 10 mg/day was effective when administered at least 30 minutes before the first food or beverage of the day.

Therefore, bioavailability and therapeutic response should be similar to that seen in these studies if alendronate **10 mg** is taken as directed (see **"DOSAGE AND DIRECTIONS FOR USE"**).

Bioavailability is negligible whether alendronate is administered with or up to two hours after a standardised breakfast.

When alendronate is taken with coffee or citrus juice, bioavailability is reduced by 60 %.

Oral prednisone (20 mg three times daily for five days) administered in healthy subjects, did not produce a clinically meaningful change in the oral bioavailability of alendronate (a mean increase ranging from 20 to 44 %).

Distribution

Alendronate is transiently distributed to soft tissue and then rapidly redistributed to bone or excreted in the urine. The volume of distribution is at least 28 l in humans.

Protein binding

Approximately 78 % in human plasma.

Elimination

Following a single intravenous dose of 10 mg alendronate, the renal clearance was 71 ml per minute. Within 6 hours the plasma concentrations fell by more than 95 %. The terminal half-life in humans is estimated to exceed 10 years, reflecting release of alendronate from the skeleton.

There is no evidence that alendronate is metabolised in humans.

INDICATIONS

OSSADURA is indicated

- for the treatment of postmenopausal osteoporosis to reduce the risk of fractures, including those of the hip and spine (vertebral compression fractures).
- to treat and reduce the risk of glucocorticoid induced osteoporosis in postmenopausal women not receiving oestrogen.
- for the treatment of primary/hypogonadal osteoporosis in men and to reduce the risk of vertebral fractures.

CONTRA-INDICATIONS

Hypersensitivity to alendronate or any other components of the formulation.

Severe renal function impairment when creatinine clearance is less than 35 ml/minute.

Abnormalities of the oesophagus which delay oesophageal emptying such as stricture or achalasia.

The inability to stand or sit upright for 30 minutes after taking the medicine.

Paediatric age group: Safety and efficacy have not been established.

Pregnancy and lactation.

Hypocalcaemia (see Warnings and Special Precautions)

WARNINGS

A dental examination with appropriate preventive dentistry should be considered prior to treatment with bisphosphonates, including **OSSADURA** , in patients with concomitant risk factors (e.g. cancer, chemotherapy, corticosteroids, poor oral hygiene).

While on treatment, these patients should avoid invasive dental procedures if possible.

For patients who develop osteonecrosis of the jaw while on **OSSADURA therapy**, dental surgery may exacerbate the condition. For patients requiring dental procedures, there are no data available to suggest whether discontinuation of **OSSADURA treatment** reduces the risk of osteonecrosis of the jaw. Clinical judgement of the treating doctor should guide the management plan of each patient based on individual benefit/risk assessment.

Hypocalcaemia and vitamin D deficiency should be corrected before starting **OSSADURA** therapy, as **OSSADURA may** exacerbate these conditions.

The risk benefit should be considered in patients suffering from upper gastrointestinal diseases, such as dysphagia, duodenitis, gastritis, ulcers or symptomatic oesophageal conditions, because of possible irritant effects of **OSSADURA** on the upper gastrointestinal mucosa and a potential for worsening of the underlying disease.

Oesophageal adverse experiences, such as oesophagitis, oesophageal ulcers and oesophageal erosions, infrequently followed by oesophageal stricture, have been reported in patients receiving treatment with **OSSADURA** in some cases these have been severe and require hospitalisation. Doctors should therefore be alert to any signs or symptoms signalling a possible oesophageal reaction and patients should be instructed to discontinue **OSSADURA** 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 **OSSADURA** and/or who fail to swallow it with a full glass of water, and/or who continue to take **OSSADURA** after developing symptoms suggestive of oesophageal irritation. Therefore, it is very important that the full dosing instructions are provided to, and understood by, the patient (see **"DOSAGE AND DIRECTIONS FOR USE"**).

INTERACTIONS

An increased incidence of upper gastrointestinal adverse events may occur in patients taking **OSSADURA** concomitantly with NSAIDs.

There may be additive hypocalcaemic effects with aminoglycosides.

Substances, such as calcium supplements, osmotic laxatives, antacids, food and beverages will interfere with the absorption of **OSSADURA** . Patients are advised to wait at least 30 minutes after taking **OSSADURA** before taking any other medication, or food.

No adverse experiences attributable to the concomitant use of alendronate and oestrogen (intravaginal, transdermal, or oral) in postmenopausal women have been identified.

PREGNANCY AND LACTATION

The safety of **OSSADURA** has not been established in pregnancy or lactation.

DOSAGE AND DIRECTIONS FOR USE

Treatment of postmenopausal osteoporosis:

The recommended dosage is 10 mg once a day.

Treatment and reduction of the risk of glucocorticoid-induced osteoporosis in postmenopausal women not receiving oestrogen:

The recommended dosage is 10 mg once a day.

Treatment of primary/hypogonadal osteoporosis in men:

The recommended dosage is 10 mg once a day.

Treatment of postmenopausal osteoporosis:

The recommended dosage is one 70 mg tablet once weekly.

Treatment of primary/idiopathic osteoporosis in men:

The recommended dosage is one 70 mg tablet once weekly.

PRODUCT NAME] must be taken at least one-half hour before the first food, beverage, or medication of the day with plain water only. Other beverages (including mineral water), food, and some medications are likely to reduce the absorption of **OSSADURA** (see **"INTERACTIONS"**).

Patients should take calcium and vitamin D supplements if their dietary intake is inadequate (see **"SPECIAL PRECAUTIONS"**). These should be taken at least 30 minutes after taking **OSSADURA**

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Patients should be advised to remain in an upright position for 30 minutes after taking **OSSADURA** tablets.

To facilitate delivery to the stomach and thus reduce the potential for oesophageal irritation, **OSSADURA** should only be swallowed upon arising for the day with a **full** glass of water and patients should not lie down for at least 30 minutes **and** until after their first food of the day. **OSSADURA** should not be taken at bedtime or before arising for the day. Failure to follow these instructions may increase the risk of oesophageal adverse experiences (see **"Special Precautions"**).

No dosage adjustment is necessary for the elderly or for patients with mild-to-moderate renal insufficiency (creatinine clearance 30 to 80 ml/min) (see **"CONTRA-INDICATIONS"**.)

SIDE-EFFECTS AND SPECIAL PRECAUTIONS

Side-effects:

The following adverse reactions have been reported with **OSSADURA** :

Hepato-biliary disorders

Less frequent: Raised liver enzymes, hepatitis, hepatocellular damage

Blood and lymphatic system disorders

Less frequent: Anaemia, leucopenia, thrombocytopenia

Renal and urinary disorders

Less frequent: Renal Failure

Cardiac disorders

Less frequent: Artrial fibrillation

Neoplasms benign malignant (including cysts and polyps)

Less frequent: Oesophageal cancer

Metabolism and nutrition disorders:

Less frequent:

Symptomatic hypocalcaemia, generally in association with predisposing conditions (see **"Special Precautions"**) hypophosphataemia.

Nervous system disorders:

Frequent:

Headache

Eye disorders:

Less frequent:

Uveitis, scleritis

Gastrointestinal disorders:

Frequent:

Abdominal pain, dyspepsia, oesophageal ulcer, dysphagia, abdominal distention, oesophagitis, oesophageal erosions, nausea, vomiting, constipation, diarrhoea, flatulence, acid regurgitation and melaena.

Less frequent:

Oesophageal stricture, oropharyngeal ulceration, gastritis, gastric and duodenal ulcers, some severe and with complications, oesophageal perforations.

(See **"Special Precautions"** and **"DOSAGE AND DIRECTIONS FOR USE"**).

Skin and subcutaneous tissue disorders:

Less frequent:

Rash (occasionally with photosensitivity), erythema and pruritus, severe skin reactions including Stevens-Johnson syndrome and toxic epidermal necrolysis.

Musculoskeletal, connective tissue and bone disorders:

Frequent:

Musculoskeletal (bone, muscle or joint) pain, myalgia.

Less frequent:

Osteonecrosis of the jaw (see **"WARNINGS"**), synovitis,

Immune system disorders:

Less frequent:

Hypersensitivity reactions, including urticaria and angioedema

General disorders and administrative site conditions:

Less frequent:

Malaise, fever

Special Precautions:

To facilitate delivery to the stomach and therefore reduce the potential for oesophageal irritation, patients should be instructed to swallow **OSSADURA** with a **full** glass of water and not to lie down for at least 30 minutes **and** until after their first food of the day.

Patients should not chew or suck on the tablet because of a potential for oropharyngeal ulceration.

Patients should be specifically instructed not to take **OSSADURA** 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 **OSSADURA** and consult their doctor.

Causes of osteoporosis other than oestrogen deficiency, aging and glucocorticoid use should be considered.

Due to the positive effects of **OSSADURA** to increase bone mineral, small, asymptomatic decreases in serum calcium and phosphate may occur, especially in patients receiving glucocorticoids, in whom calcium absorption may be decreased.

Ensuring adequate calcium and vitamin D intake is especially important in patients receiving glucocorticoids.

Use in the Elderly:

There is no age-related difference in the efficacy or safety profiles of **OSSADURA** .

Effects on ability to drive and use machines:

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

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT

Hypocalcaemia, hypophosphataemia and upper gastrointestinal adverse events, such as upset stomach, heartburn, oesophagitis, gastritis, or ulcer, may result from oral overdosage. The administration of milk and antacids may be of benefit.

Because of the risk of oesophageal irritation, vomiting should not be induced. Keep the patient in an upright position.

IDENTIFICATION

OSSADURA 10 mg: White to off-white, round, biconvex, uncoated tablets, debossed with 'F' on one side and '18' on the other side.

OSSADURA 70 mg: White to off-white, oval shaped, biconvex, uncoated tablets, debossed with 'F' on one side and '21' on the other side.

PRESENTATION

OSSADURA 10 mg:

Tablets are packed in printed aluminium foil with heat seal lacquer and clear PVC laminated with aclar. Each blister contains 10 tablets.

Pack size: 30's – Each carton contains 3 blisters of 10 tablets each.

Tablets are packed in 40 ml white opaque HDPE containers with white opaque polypropylene closures with induction sealing wad. Each container contains 30 tablets.

Pack size: 30's – One HDPE container contains 30 tablets.

OSSADURA 70 mg:

Tablets are packed in printed aluminium foil with heat seal lacquer and clear PVC laminated with aclar. Each blister contains 4 tablets.

Pack size: 4's – Each carton contains 1 blister of 4 tablets each.

STORAGE INSTRUCTIONS

Store in a dry place at or below 25 °C. Do not remove blisters from carton until required for use. Keep original containers well closed.

KEEP OUT OF REACH OF CHILDREN

REGISTRATION NUMBER

OSSADURA 10 mg: 45/3.2/0582

OSSADURA 70 mg: 45/3.2/0583

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION

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