APPROVED PROFESSIONAL INFORMATION

SCHEDULING STATUS

S3

PROPRIETARY NAME (and dosage form)

ETANORDES 35 mg TABLETS

COMPOSITION

Each film-coated tablet contains risedronate sodium hemipentahydrate 35 mg equivalent to 32.5 mg risedronic acid.

Contains lactose monohydrate, cellulose microcrystalline, crospovidone XL, hydroxy propyl cellulose (low viscosity grade), magnesium stearate and opadry brown.

The coating material of **ETANORDES 35 mg TABLETS** contains colloidal anhydrous silica, hydroxypropyl cellulose, hypromellose, iron oxide red, iron oxide yellow, macrogol / PEG 400, macrogol / PEG 8000 and titanium dioxide.

PHARMACOLOGICAL CLASSIFICATION

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

PHARMACOLOGICAL ACTION

Pharmacodynamic properties:

Risedronate sodium is a pyridinyl bisphosphonate that binds to bone hydroxyapatite and inhibits osteoclast-mediated bone resorption, while bone formation is preserved. In preclinical studies, risedronate demonstrated anti-osteoclast and antiresorptive activity, dose-dependently.

The activity of risedronate sodium was confirmed by bone marker measurements.

Pharmacokinetic properties:

Absorption: After an oral dose absorption has occurred throughout the upper gastrointestinal tract.

Absorption is independent of dose over the range studied (single dose study, 2,5 to 30 mg; multiple dose studies, 2,5 to 5 mg daily and up to 50 mg dosed weekly).

Mean oral bioavailability of the tablet is 0, 63 % and is decreased significantly when risedronate sodium is administered with food. Bioavailability was similar in men and women.

Distribution: Preclinical studies in rats and dogs dosed intravenously with single doses of [^{14}C]-risedronate sodium, indicate that approximately 60 % of the dose is distributed to bone. The remainder of the dose is excreted in the urine. The mean steady state volume of distribution is 6, 3 l/kg in humans. Human plasma protein binding of the medicine is about 24 %.

Metabolism: There is no evidence of systemic metabolism of risedronate sodium.

Elimination: Approximately half of the absorbed dose is excreted in urine within 24 hours and 85 % of an intravenous dose is recovered in the urine over 28 days. Mean renal clearance is 105 ml/min and mean total clearance is 122 ml/min, with the difference primarily reflecting non-renal clearance or clearance due to adsorption to bone. The renal clearance is not concentration dependent and there is a linear relationship between renal clearance and creatinine clearance.

Unabsorbed risedronate is eliminated unchanged in faeces. Once risedronate sodium is absorbed, the serum concentration-time profile is multi-phasic with an initial half-life of about 1, 5 hours and a terminal exponential half-life of 480 hours.

Special populations: Patients with renal impairment and the elderly (see **"Dosage and Directions for Use"**).

INDICATIONS

Treatment of osteoporosis in postmenopausal women, in combination with calcium 500 -1000 mg per day. Additional administration of vitamin D should be considered when a deficiency might be expected.

CONTRA-INDICATIONS

Known hypersensitivity to risedronate sodium or any ingredient of this product.

Hypocalcaemia (see **"Warnings and Special Precautions"**).

Advanced renal impairment: creatinine clearance < 30 ml/min (see **"Warnings and Special Precautions"**).

WARNINGS AND SPECIAL PRECAUTIONS

ETANORDES 35 mg TABLETS may cause upper gastro-intestinal disorders such as dysphagia, oesophagitis, oesophageal ulcer and gastric ulcer. Therefore, patients should pay attention to the dosing instructions (see **"Dosage and Directions for Use"**). Prescribers should emphasise the importance of the dosing instructions to patients who have a history of oesophageal disorders and upper gastrointestinal disorders.

In order to facilitate delivery to the stomach and minimise the possibility of gastrointestinal adverse effects, patients should take **ETANORDES 35 mg TABLETS** while in an upright position (standing or sitting) with a full glass of plain water and should avoid lying down for 30 minutes after taking **ETANORDES 35 mg TABLETS**.

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 3 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 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. Bisphosphonate treatment should be stopped in patients with stress fractures and they should receive appropriate orthopaedic care.

Osteonecrosis of the jaw:

Osteonecrosis of the jaw generally associated with tooth extraction and/or local infection (including osteomyelitis) has been reported in patients with cancer receiving treatment regimens including primarily 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 **ETANORDES 35 mg TABLETS**.

A dental examination with appropriate preventative dentistry should be considered prior to treatment

with bisphosphonates, such as **ETANORDES 35 mg TABLETS** in patients with concomitant risk factors (e.g. cancer, chemotherapy, radiotherapy, 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 bisphosphonate therapy, such as **ETANORDES 35 mg TABLETS**, 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 judgment of the treating doctor should guide the management plan of each patient based on an individual benefit/risk assessment.

ETANORDES 35 mg TABLETS is not recommended in patients with severe renal impairment (creatinine clearance < 30 ml/min).

Hypocalcaemia and other disturbances of bone and mineral metabolism should be effectively treated before starting **ETANORDES 35 mg TABLETS** therapy. Asymptomatic, small decreases in serum calcium and phosphorus levels have been observed in some patients.

Adequate intake of calcium and vitamin D is important.

Patients should receive supplemental calcium and vitamin D if dietary intake is inadequate.

Foods, drinks (other than plain water) and medicinal products containing polyvalent cations (such as calcium, magnesium, iron and aluminium) may interfere with the absorption of **ETANORDES 35 mg TABLETS** and should not be taken at the same time. Therefore, to achieve the proven benefits of **ETANORDES 35 mg TABLETS**, patients should take the tablet either, at least 30 minutes before the first food, medicinal product or drink (other than plain water) of the day or, at least two hours away from food or drink at any other time of the day.

Treatment with **ETANORDES 35 mg TABELTS** is not known to affect your ability to drive and use machines.

ETANORDES 35 mg TABLETS contains lactose. Patients with rare hereditary problems of galactose intolerance, lapp lactase deficiency, or glucose-galactose malabsorption should not take **ETANORDES 35 mg TABLETS**.

INTERACTIONS

ETANORDES 35 mg TABLETS has been used with aspirin and NSAIDs.

If considered appropriate, **ETANORDES 35 mg TABLETS** may be used concomitantly with Hormone Replacement Therapy.

Concomitant use of medications containing polyvalent cations (e.g. calcium, magnesium, iron and aluminium) interferes with the absorption of **ETANORDES 35 mg TABLETS** (see **"Warnings and Special Precautions"**).

ETANORDES 35 mg TABLETS is not systematically metabolised, does not induce cytochrome P450 enzymes and has low protein binding.

PREGNANCY AND LACTATION

The safety of **ETANORDES 35 mg TABLETS** in pregnant and lactating women has not been established.

DOSAGE AND DIRECTIONS FOR USE

Dosage:

Adults: The recommended dose is one 35 mg tablet orally, once a week. The tablet should be taken on the same day of each week.

Foods, drinks (other than plain water) and medicinal products containing polyvalent cations (such as calcium, magnesium, iron and aluminium) may interfere with the absorption of **ETANORDES 35 mg TABLETS** and should not be taken at the same time. Therefore, **ETANORDES 35 mg TABLETS** should be taken either, at least 30 minutes before the first food, medicinal product or drink (other than plain water) of the day or, at least two hours away from food or drink at any other time of the day and at least 30 minutes before going to bed.

Patients should be instructed that if a dose is missed, one **ETANORDES 35 mg TABLETS** should be taken on the day that the tablet is remembered. Patients should then return to taking one tablet once a week on the day the tablet is normally taken. Two tablets should not be taken on the same day.

The tablets must be swallowed whole and not sucked or chewed.

Patients should take **ETANORDES 35 mg TABLETS** while in an upright position with a glass of plain water (≥ 120 ml) to aid delivery to the stomach. Patients should not lie down for 30 minutes after taking

the tablet (see **"Warnings and Special Precautions"**).

Elderly: No dosage adjustment is necessary since bioavailability and disposition were similar in elderly (> 60 years of age) compared to younger subjects.

Renal impairment: No dosage adjustment is necessary in patients with creatinine clearance ≥ 30 ml/min. There is no clinical data in patients with severe renal impairment (creatinine clearance < 30 ml/min), so no dosage recommendation can be made for this population.

Children: Safety and efficacy of **ETANORDES 35 mg TABLETS** have not been established in children and growing adolescents.

SIDE-EFFECTS

The following adverse experiences have been reported:

Infections and infestations:

Frequent: Infection.

Less Frequent: Urinary tract infection.

Blood and the lymphatic system disorders:

Less frequent: Anaemia, Leucopenia.

Eye disorders:

Frequent: Amblyopia, dry eyes.

Less Frequent: Iritis.

Ear and labyrinth disorders:

Frequent: Tinnitus.

Vascular disorders:

Frequent: Hypertension.

Respiratory, thoracic and mediastinal disorders:

Frequent: Bronchitis, pharyngitis, sinusitis.

Less frequent: Pneumonia.

Gastrointestinal disorders:

Frequent: Dyspepsia, nausea, belching, abdominal pain, constipation, diarrhoea, colitis.

Less Frequent: Oesophagitis, oesophageal ulcer, gastritis, dysphagia, duodenitis, glossitis, oesophageal stricture, vomiting.

Nervous system disorders:

Frequent: Headache, dizziness.

Less frequent: Syncope.

Psychiatric disorders:

Less frequent: Anxiety.

Immune system disorders:

Less Frequent: Angioedema.

Hepato-biliary disorders:

Frequency unknown: Abnormal liver function tests.

Musculoskeletal, connective tissue and bone disorders:

Frequent: Musculoskeletal pain, arthralgia, bone pain, joint disorder, leg cramps, myasthenia.

Less frequent: Bursitis, *osteonecrosis of the jaw, atypical fracture of the femur (see **"Warnings and Special Precautions"**).

Skin and subcutaneous tissue disorders:

Less Frequent: Hypersensitivity and skin reactions, including generalised rash, bullous skin reactions, pruritus.

General disorders and administrative site conditions:

Frequent: Back pain, pain, asthenia, chest pain, flu-like syndrome.

Less frequent: Neoplasm.

Investigations:

Frequency unknown: Decreases in serum calcium and phosphate levels.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT

Reduction in serum calcium following overdose may be expected. Signs and symptoms of hypocalcaemia may occur.

Milk or antacids containing magnesium, calcium or aluminium should be given to bind **ETANORDES 35 mg TABLETS** and reduce absorption of risedronate. In cases of substantial overdose, gastric lavage may be considered to remove unabsorbed medicine.

IDENTIFICATION

Light orange coloured, circular shaped, film-coated biconvex tablets debossed with 'F27' on one side and plain on the other side.

PRESENTATION

Blister Pack:

Tablets are packed in 250 micron clear PVC, 25 micron PE and 90 gsm PVdC and printed 25 micron aluminium foil with 7 gsm heat seal lacquer. Each blister contains 4 tablets.

Pack size: **4's** – Each carton contains one blister of 4 tablets.

STORAGE INSTRUCTIONS

Store at or below 30 °C.

Do not remove the blisters from the carton until required.

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER

45/3.2/0868

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

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29 July 2019

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