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ETIDRATE

Disodium Etidronate

Presentation

200 mg tablets: White, rectangular-shaped, biconvex tablets with "ED 200" on one side and "G" on the other.

400 mg tablets: White, capsule-shaped, tablets with "ED 400" on one side and "G" on the other.

Uses

Actions

Disodium etidronate acts primarily on bone. It can modify the crystal growth of calcium hydroxyapatite in vitro by chemisorption onto the crystal surface. Depending on concentration, disodium etidronate primarily inhibits either crystal resorption or crystal growth. The exact mechanism of in vivo activity is uncertain and may additionally involve direct effects on cellular metabolic processes.

Serum phosphate elevations have been observed when disodium etidronate is administered at daily doses of 10mg/kg body weight/day or above and occasionally at 5mg/kg/day. This has not been found to be an indication for discontinuing therapy. This medicine-related elevation appears to be the result of increased tubular reabsorption of phosphate by the kidney, and serum values in excess of 7% have been observed with high doses. No adverse effects of disodium etidronate-induced hyperphosphataemia have been found. Serum phosphate levels generally return to normal 2-4 weeks after stopping medication. Disodium etidronate therapy is not accompanied by clinically significant changes in serum parathyroid hormone or serum calcium levels.

Osteoporosis

Osteoporosis is an age-related disorder characterised by a decrease in bone mass and an increased susceptibility to fracture. Disodium etidronate works directly to increase mineralised bone mass. By timing delivery and withdrawal, disodium etidronate acts to modulate osteoclasts to reduce the mean resorption depth of the affected basic multicellular units (BMU). Two weeks of disodium etidronate treatment (400mg/day) is repeated every 13 weeks. During the 11 week drug-free period adequate amounts of calcium are supplemented to ensure proper intake of this essential bone mineral.

Reducing bone turnover and resorptive cavity depth results in the maintenance of existing trabecular structure. Clinically, in responsive patients, this produces an increase in bone mass. Data (up to two years) demonstrate a reduced risk of vertebral fracture and a slowing of the progression of vertebral deformity. Based on bone biopsy data, disodium etidronate intermittent cyclical therapy, beyond 16 cycles (4 years), was associated with an increased prevalence of mild to moderate osteomalacia and peritrabecular fibrosis. These changes have not been associated with any detectable clinical consequences.

Paget's Disease

Paget's disease is an idiopathic bone disorder characterised by abnormal and accelerated bone resorption and formation in one or more bones. The extent and severity of the disease is highly variable. Characteristic symptoms may be bone pain, varying degrees of bone deformity, neurologic disorders, and less frequently, vascular disorders. Cardiac output may be abnormally elevated secondary to the increased vascularity associated with Paget's disease. Increased bone resorption results in increased urinary excretion of hydroxyproline and increased bone formation is reflected by increased levels of serum alkaline phosphatase.

Disodium etidronate slows the rate of bone turnover (bone resorption and new bone accretion) in Pagetic bone lesions and in the normal remodelling process.

Histologic examination of bone from Pagetic patients on disodium etidronate therapy shows a reduction in the excessive cellular activity accompanied by a suppression of bone resorption and accretion and a return towards normal of the histologic patterns. Accumulation of unmineralised osteoid has been frequently observed in patients treated with a dose of 20mg/kg/day and in some patients after six months of therapy at lower doses (see Warnings and Precautions - "Paget's Disease").

Disodium etidronate therapy affects several clinical abnormalities seen in patients with Paget's disease: lowering elevated urinary hydroxyproline excretion, lowering elevated serum alkaline phosphatase, and reducing the uptake of radionuclide bone imaging agents at active Pagetic bone sites. These changes are consistent with a reduction in bone turnover rate, which has been demonstrated in man by calcium kinetic and balance studies and by morphometric studies of bone. In addition, disodium etidronate therapy reduces vascularity of Pagetic bone, reduces abnormally elevated cardiac output associated with active Paget's disease, and lowers the temperature over superficially located Pagetic lesions. These actions may be accompanied by symptomatic improvement, including reduced bone pain. The first evidence of therapeutic response to disodium etidronate in Paget's disease, reduction of urinary hydroxyproline excretion, usually occurs after one to three months of medication.

Heterotopic Ossification

Disodium etidronate chemisorbs to calcium hydroxyapatite crystals, blocking further crystal growth and mineralisation. This is thought to be the mechanism of action, which prevents or retards heterotopic bone formation during the active stage.

1. Heterotopic Ossification due to Spinal Cord Injury

Heterotopic ossification following spinal cord injury commonly occurs in about 40% of patients. Although a complete understanding of the sequence and nature of events which lead to heterotopic bone masses in soft tissue is unknown, the formation is the result of metaplastic osteogenesis and mineralisation. Heterotopic ossification appears to be most active during the period immediately following injury.

2. Heterotopic Ossification Complicating Total Hip Replacement

The incidence of heterotopic ossification following total hip arthroplasty varies with its definition and classification. It is reported as occurring as a complication in about 20% of patients. In studies with disodium etidronate, about 50% of placebo treated patients were reported to develop radiographic evidence of heterotopic ossification. Although the aetiology of this heterotopic ossification remains undefined, local trauma is a known associated factor and may be the inciting factor. Heterotopic ossification following total hip arthroplasty appears radiographically as early as three weeks post-operatively, with the peak incidence occurring 3-8 weeks post-operatively.

Retreatment has not been studied. There is no evidence that disodium etidronate therapy will affect mature heterotopic bone.

Pharmacokinetics

Disodium etidronate is not metabolised. Patients absorb an average of about 1% of an oral dose of 5 mg/kg body weight/day. The absorption increases with dose level to about 2.5% at 10 mg/kg/day and 6% at 20mg/kg/day. Most of the absorbed drug is cleared from the blood within six hours. In normal subjects, plasma half-life ($t_{1/2}$) of etidronate, based on non-compartmental pharmacokinetics, is 6.0 (0.7 hours) Within 24 hours about one-half of the absorbed dose is excreted in the urine. The remainder is chemically absorbed on the bone and is slowly eliminated. Absorption varies appreciably between individuals. Unabsorbed etidronate is excreted in the faeces.

Indications

Osteoporosis

Disodium etidronate is indicated for the treatment of osteoporosis in both men and women. This includes the prevention and treatment of corticosteroid induced osteoporosis and the prevention and treatment of osteoporosis in postmenopausal women.

Paget's Disease

Disodium etidronate is indicated for the treatment of symptomatic Paget's disease of bone (osteitis deformans) when other therapy is considered inappropriate or cannot be tolerated. Effectiveness has been demonstrated primarily in patients with polyostotic Paget's disease with symptoms of pain and with clinically significant elevations of urinary hydroxyproline and serum alkaline phosphatase. In patients treated with disodium etidronate at the dose of 5mg/kg/day, the elevated urinary hydroxyproline and serum alkaline phosphatase decreased by 30% or more in about 4 out of 5 patients. Hydroxyproline either returned to normal or was decreased by at least 50% in about 3 out of 5 patients and alkaline phosphatase in about one-half of the patients.

In controlled studies, approximately 3 out of 5 patients experienced decreased pain and/or improved mobility. Two out of 5 patients in the placebo group showed similar subjective improvement. Objective measurements in disodium etidronate-treated patients have shown reductions of elevated cardiac output in about 2 out of 3 patients. Reductions in elevated skin temperature over Pagetic lesions have also been measured. The number of treated patients in these categories is still too small to predict with certainty how likely such a result will be in any given patient. Objective evidence of hearing improvement has not been demonstrated.

The majority of patients with localised, especially monostatic bone disease, do not develop symptoms and most patients with mild symptoms can be managed with analgesics. There is no evidence that the prophylactic use of disodium etidronate is beneficial in asymptomatic patients, although treatment may be considered in exceptional circumstances in which there is extensive involvement of the skull or the vertebrae with the prospect of irreversible neurologic damage. In these instances, treatment would be based on the demonstrated effect of disodium etidronate on Pagetic bone rather than on clinical studies in such asymptomatic patients.

Heterotopic Ossification

a) Heterotopic Ossification due to Spinal Cord Injury

Disodium etidronate is indicated in the prevention and treatment of heterotopic ossification due to spinal cord injury.

In placebo-controlled studies among spinal cord injured patients, disodium etidronate therapy resulted in significant reduction in the incidence of heterotopic bone; 4 out of 69 (6%) disodium etidronate-treated patients developed heterotopic ossification versus 17 out of 63 (27%) placebo-treated patients.

In those patients with radiographic evidence of early heterotopic ossification or who developed masses while on therapy, disodium etidronate was effective in retarding the progression of these immature masses. Progression was observed in 6 out of 81 (7%) disodium etidronate-treated patients who developed heterotopic ossification versus 26 out of 76 (34%) placebo-treated patients.

Disodium etidronate has been shown to reduce significantly the severity of clinically important heterotopic ossification masses, i.e. masses of sufficient size to restrict range of motion, require surgical removal or be of other clinical significance. Follow up data from controlled studies are inadequate to define the post-treatment benefits of disodium etidronate.

b) Heterotopic Ossification Complicating Total Hip Replacement

Disodium etidronate is indicated in the prevention and treatment of heterotopic ossification following total hip replacement.

In placebo-controlled studies, among patients undergoing total hip replacement, disodium etidronate significantly reduces the incidence and severity of heterotopic bone. At the end of the medication

period 18 out of 68 (27%) disodium etidronate-treated patients versus 37 out of 74 (50%) placebo-treated patients had radiographic evidence of heterotopic ossification. The average cross sectional area of heterotopic bone was about two and one half times greater in placebo-treated patients.

Among patients with no pre-operative heterotopic bone, the incidence at the end of the medication period was 17% (8 out of 48) in disodium etidronate-treated patients versus 37% (19 out of 51) in placebo-treated patients; in observations lasting up to one year after surgery, the area of heterotopic bone was again about two and one half times greater in placebo-treated patients than disodium etidronate-treated patients.

These effects, including post-medication reduction in severity, were particularly evident in patients with osteoarthritis and traumatic arthritis who had no evidence of heterotopic ossification prior to surgery.

Disodium etidronate reduces the incidence of clinically significant heterotopic lesions, which are of sufficient size to restrict range of motion or require re-operation. Two out of 68 (3%) disodium etidronate-treated patients versus 12 out of 74 (16%) placebo-treated patients had significant heterotopic bone masses at the end of the medication period. This difference tends to persist up to one year after surgery in patients with no evidence of heterotopic ossification pretreatment. Disodium etidronate retards the progression of heterotopic ossification. Among patients with heterotopic lesions prior to surgery, disodium etidronate significantly reduces the severity of heterotopic bone that may recur during the medication period. This benefit tends to be maintained following cessation of medication.

In controlled studies, no problems relating to loosening of the prosthetic devices have been encountered. The incidence of migration of the trochanter has not been observed to be increased with disodium etidronate therapy.

Dosage and Administration

Disodium etidronate should be taken as a single, oral, daily dose. However, should gastrointestinal discomfort occur, the dose may be divided. To maximise absorption, patients should avoid taking the following items within 2 hours of dosing:

Foods, especially those high in calcium, such as milk products. Vitamins with mineral supplements or antacids which are high in metals such as calcium, iron, magnesium or aluminium.

Osteoporosis

400mg/day (5-10mg/kg/day) for 14 days followed by a 76 day period of calcium (the minimum recommended supplement is 500mg/day of elemental calcium). Patients should maintain an adequate nutritional base. This 90 day cycle is repeated as prescribed by the physician. Calcium should not be given concurrently with disodium etidronate.

The optimum duration of therapy is as yet still to be determined. However, current available data support the safety of this treatment for up to 3 years.

Paget's Disease

Initial Treatment Guidelines

The recommended initial dose of disodium etidronate for most patients is 5mg/kg body weight/day, not to exceed a period of six months. Doses above 10mg/kg/day should be reserved for use when there is an over-riding requirement for suppression of increased bone turnover associated with Paget's disease or when the patient requires more prompt reduction of elevated cardiac output. Treatment with doses above 10mg/kg/day should be approached cautiously and should not exceed three months duration. Doses in excess of 20mg/kg/day are not recommended.

Urinary hydroxyproline excretion and/or serum alkaline phosphatase levels should be monitored periodically during the course of disodium etidronate therapy.

Retreatment Guidelines

Retreatment should be undertaken only after a drug-free period of at least three months and after it is evident that reactivation of the disease has occurred and biochemical indices of the disease have become substantially re-elevated or approach pretreatment values (approximately twice the upper limit of normal or 75% of pretreatment values). In no case should duration of retreatment exceed the maximum duration of the initial treatment. Premature retreatment should be avoided. In clinical trials the biochemical improvements obtained during disodium etidronate therapy have generally persisted for a period of three months to, in some cases, almost a year after disodium etidronate withdrawal.

Heterotopic Ossification

a) Heterotopic Ossification Due to Spinal Cord Injury

The recommended dose of disodium etidronate is 20mg/kg/day for 2 weeks followed by 10mg/kg/day for 10 weeks. The total treatment period is 12 weeks.

This recommended dosing regimen should be instituted as soon as is medically feasible following the injury, preferably prior to any radiographic evidence of heterotopic ossification. Retreatment has not been studied since the heterotopic ossification process is most active during the period immediately following injury. There is no evidence that disodium etidronate therapy will affect mature heterotopic bone.

Retreatment has not been studied. There is no evidence that disodium etidronate therapy will affect mature heterotopic bone.

b) Heterotopic Ossification Complicating Total Hip Replacement

The recommended dose is 20mg/kg/day for one month pre-operatively followed by 20mg/kg/day for three months post-operatively. The total treatment period is four months. Placebo-controlled studies have shown that changing the dose regimen from 20mg/kg/day for three months post-operatively to 10mg/kg/day for six months post-operatively resulted in reduced efficacy in the prevention of heterotopic ossification, and there was no statistically significant difference between the placebo- and disodium etidronate-treated groups.

Contraindications

General

Disodium etidronate is contraindicated for patients with known hypersensitivity to disodium etidronate and for patients suspected of having clinically overt osteomalacia, which should be treated prior to considering disodium etidronate therapy.

Osteoporosis and Heterotopic Ossification

Clinical trials have demonstrated no absolute contraindications.

Paget's Disease

At doses of 20 mg/kg/day, disodium etidronate usually stops mineralisation of the new bone in Pagetic lesions. Even on low dose therapy careful radiological studies indicate that osteolytic lesions may progress. Therefore, disodium etidronate should not be used in patients with significant lytic lesions or with lytic lesions involving crucially situated bones.

Warnings and Precautions

General

The physician should adhere to the recommended dose regimen in order to avoid overtreatment with disodium etidronate (see Adverse Effects).

Patients should maintain an adequate nutritional status, and particularly, an adequate intake of calcium and vitamin D. However, calcium can reduce the absorption of etidronate disodium and, therefore, should be avoided within 2 hours (before and after) of dosing with disodium etidronate (see Dosage and Administration). Patients with restricted vitamin D and calcium intake may be particularly sensitive to medicines that affect calcium homeostasis and should be closely followed while under treatment with disodium etidronate.

There are no data concerning patients with renal impairment. Disodium etidronate therapy has been withheld from patients with enterocolitis because at a dose of 20mg/kg/day, and occasionally at lower doses, the frequency of bowel movements and diarrhoea has increased.

Disodium etidronate is not metabolised and is excreted intact via the kidney; therefore, treatment of patients with impaired renal function should be undertaken very cautiously if at all. Serum creatinine levels should be closely monitored in patients with renal impairment. In patients with impaired renal function or a history of kidney stone formation, serum and urinary calcium should be monitored regularly to detect occurrence of hypercalcaemia or hypercalciuria.

In patients receiving disodium etidronate, there have been rare reports of leucopenia, agranulocytosis and pancytopenia; however a causal relationship has not been established.

Osteoporosis

The administration of calcium and disodium etidronate concomitantly should be avoided as calcium can reduce the absorption of disodium etidronate.

The efficacy and safety of etidronate in the treatment of postmenopausal osteoporosis has been established using intermittent cyclical therapy. Continuous administration of etidronate should be avoided, as osteoid (demonstrating mineralisation) may accumulate at doses of 10-20 mg/kg/day of chronic, continuous dosing.

Paget's Disease

When administered at doses of 20mg/kg/day, disodium etidronate suppresses bone turnover and essentially stops mineralisation of new bone in Pagetic lesions and, to a lesser extent, in the uninvolved skeleton. Mineralisation of Pagetic lesions has been observed to occur normally after discontinuation of the medicine.

Disodium etidronate retards mineralisation of osteoid laid down during the bone accretion process. This effect is dose and time dependent. There may be an overlap of beneficial inhibition of bone resorption and mineralisation inhibition effects in some patients at higher doses. Extended periods of medication should be approached cautiously, and the treatment of patients with impaired renal function should be undertaken very cautiously, if at all.

Patients with predominantly lytic lesions should be monitored radiographically and biochemically to permit termination of etidronate disodium in those patients unresponsive to treatment.

In Paget's patients, the response to therapy may be of slow onset and may continue for months after therapy has been discontinued. Dosage should not be increased prematurely, nor should treatment be resumed before there is clear evidence of reactivation of the disease process. A drug-free interval of at least 90 days should be provided between courses of therapy.

Osteogenic sarcoma is known to be increased in Paget's disease. With or without therapy, pagetic lesions may appear radiographically to progress markedly, possibly with some loss of definition of periosteal margins. Such lesions should be evaluated carefully to permit differentiation from osteogenic sarcoma.

Increased or recurrent bone pain at existing Pagetic sites and/or the appearance of pain at sites previously asymptomatic has been reported. At the recommended dose (5 mg/kg/day) 1 out of 10 patients reported the phenomena; at higher doses the figure rose to 2 out of 10. In placebo-treated patients, the occurrence was 1 out of 15. In disodium etidronate-treated patients, the pain resolved while therapy was continued in some patients but persisted for several months in others.

Fractures are recognised as a common feature in patients with Paget's disease. The risk of fracture may be increased when disodium etidronate is taken at a dose level of 20 mg/kg/day in excess of 3 months. This risk may be greater in patients with extensive and severe disease, a history of multiple fractures, and/or rapidly advancing osteolytic lesions. It is recommended that the drug be discontinued if fractures occur and that therapy not be reinstated until fracture healing is complete.

Heterotopic Ossification Due to Spinal Cord Injury

Concomitant fractures are common in patients with spinal cord injury. In controlled studies, no problems of fracture healing or stabilisation of the spine were encountered. In cases with multiple long bone fractures, it may be advisable to delay therapy for a short time until callus formation is evidenced.

Heterotopic Ossification complicating Total Hip Replacement

There are no specific warnings to patients with patients undergoing total hip replacement.

Carcinogenicity, Mutagenicity and Impairment of Fertility

No evidence for a carcinogenic effect of etidronate disodium was found in long-term studies in mice and rats at oral doses of up to 50 and 20 mg/kg/day, respectively (ca. 30 to 40% of the maximum clinical dose based on body surface area).

Etidronate disodium was not genotoxic, as assessed *in vitro* for gene mutations and chromosomal aberrations. An *in vivo* assay of chromosomal damage (micronucleus test in Chinese hamsters) was also negative.

The effects of disodium etidronate on fertility have been studied in male and female rats. Treatment of male rats with disodium etidronate at oral doses greater than 100 mg/kg/day (ca. 1.6 times the maximum clinical dose based on body surface area) was associated with a decreased mating rate and an increased incidence of pre-implantation loss. The reproductive capacity of females was adversely affected following treatment with disodium etidronate at oral doses greater than 300 mg/kg/day (ca. 5 times the maximum clinical dose based on body surface area).

Use in Pregnancy (Category B3)

Disodium etidronate is not intended for administration to pregnant women. There are no adequate well-controlled studies in pregnant women. This medicine should be used during pregnancy only if clearly needed, when the potential benefit justifies the potential risk to the foetus.

Use in Pregnancy

Reproduction studies have been performed in rats and rabbits. Although placental transmission of the medicine was negligible, embryo-toxicity was observed in rats and the conception rate in rabbits was decreased. Treatment of pregnant rats with etidronate disodium was associated with embryofoetal toxicity and foetal bone abnormalities at oral doses greater than 300 mg/kg/day (ca. 5 times the maximum clinical dose based on body surface area). In female rabbits, the conception rate was decreased at 100 mg/kg/day PO (ca. 3 times the maximum clinical dose based on body surface area). No teratogenic effects were observed..

Use in Lactation

It is not known whether the medicine is excreted in human milk, nor whether it has a harmful effect on the newborn. Therefore it is not recommended for nursing mothers unless the benefits outweigh any potential risk.

Use in Children

Disodium etidronate is not intended for administration to children. Safety and effectiveness in children have not been fully established.

Use in the Elderly

Special Precautions related to the use of disodium etidronate in geriatric patients have not been identified. However, serum creatinine levels should be closely monitored in patients with renal impairment.

Osteonecrosis of jaw

Osteonecrosis, primarily in the jaw, has been reported in patients treated with bisphosphonates. Most cases have been in cancer patients undergoing dental procedures such as tooth extraction, but some have occurred in patients with postmenopausal osteoporosis or other diagnoses. Most reported cases have been in patients treated with bisphosphonates intravenously but some have been in patients treated orally

Dentinogenesis

The effect of prolonged treatment upon dentinogenesis has not been studied.

Information for Patients

The patient should adhere closely to the prescribed regimen

Adverse Effects

Side effects reported have been diarrhoea and nausea. The major side effect is diarrhoea affecting about 7% of placebo treated patients and 10% of patients at a dose of 5mg/kg. This incidence rises to approximately 20% in patients at 20mg/kg but can be reduced by dividing the dose.

The following events have been observed with oral or intravenous use of disodium etidronate and were thought to be possibly related to the therapy; alopecia, arthropathies including arthralgia and arthritis, burning of the tongue (glossitis). Hypersensitivity reactions, which have been reported, include skin rashes, such as follicular eruption, macular rash, maculopapular rash, erythema exudatum multiforme, angioedema, urticaria, pruritus and exacerbation of asthma. Neuropsychiatric events reported include amnesia, confusion, depression and hallucinations and paresthesias including peripheral neuropathy.

In patients receiving disodium etidronate, there have been rare reports of leucopenia, agranulocytosis and pancytopenia; however, a causal relationship has not been established. In addition exacerbation of existing peptic ulcer with perforation has been reported in a few patients.

Paget's Disease

Increased or recurrent bone pain at existing Pagetic sites and/or the appearance of pain at sites previously asymptomatic has been reported. At the recommended dose (5mg/kg/day) 1 out of 10 patients reported the phenomena; at higher doses the figure rose to 2 out of 10. In placebo-treated patients, the occurrence was 1 out of 15. In disodium etidronate-treated patients, the pain resolved while therapy was continued in some patients but persisted for several months in others.

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fractures, and/or rapidly advancing osteolytic lesions. It is recommended that the medicine be discontinued if fractures occur and that therapy not be reinstated until fracture healing is complete.

Osteoporosis

In osteoporosis clinical trials the most common side effects were diarrhoea and nausea. Reactions reported less frequently include flatulence, dyspepsia, abdominal pain, constipation and vomiting. The incidence of these events was comparable to that with placebo. In addition, four events, headache, gastritis, leg cramps and arthralgia occurred with a significantly greater incidence in patients who received disodium etidronate cyclical therapy compared with those who received placebo. All episodes of leg cramps were transient in nature, most occurred at night, and most required no treatment. All patients with arthralgia reported joint discomfort or pain that was generally mild and related to underlying osteoarthritis.

Heterotopic Ossification

There are no adverse reactions peculiar to patients with spinal cord injury or undergoing total hip replacement.

Interactions

Disodium etidronate is known to interact with calcium and other divalent or trivalent cations. (see Dosage and Administration).

There have been isolated reports of patients experiencing increases in their prothrombin times when etidronate was added to warfarin therapy. The majority of these reports concerned variable elevations in prothrombin times without clinically significant sequelae. Although the relevance of these reports and any mechanism of coagulation alterations is unclear, patients on warfarin should have their prothrombin time monitored.

Effects on Laboratory Tests

The diagnostic utility of bone-imaging agents may be impaired by current or recent etidronate use. If a patient currently or recently treated with DIDRONEL requires imaging with bone-seeking isotopes, false negative bone scans may be obtained.

Overdosage

Clinical experience with acute overdosage of disodium etidronate is extremely limited. Decreases in serum calcium following substantial overdosage may be expected in some patients. Signs and symptoms of hypocalcaemia may also occur in some of these patients. Some patients may develop vomiting. An 18 year old female who ingested an estimated single dose of 4,000-6,000mg (67-100mg/kg) of disodium etidronate was reported to be mildly hypocalcaemic (7.52mg/d or 1.87 mmol/L) and to have experienced paresthesia of the fingers. A 92 year old female who accidentally received 1,600mg of disodium etidronate per day for 3.5 days experienced marked diarrhoea and required treatment for electrolyte imbalance.

. Overdose treatment is symptomatic and supportive Standard procedures for treating hypocalcaemia, including the administration of calcium intravenously, would be expected to restore physiologic amounts of ionised calcium and to relieve signs and symptoms of hypocalcaemia..

Activated charcoal is most effective when administered within 1 hour of ingestion. In patients who are not fully conscious or have impaired gag reflex, consideration should be given to administering activated charcoal via nasogastric tube once the airway is protected. With disodium etidronate, dialysis would not be beneficial.

Contact the Poisons Information Centre for advice on the management of an overdose.

Pharmaceutical Precautions

Store below 25°C.

Medicine Classification

Prescription Medicine.

Package Quantities

200 mg: Bottles of 100 tablets.

400 mg: Bottles of 100 tablets (not marketed).

Further Information

Disodium etidronate is the disodium salt of (1-hydroxyethylidene) diphosphonic acid. The compound, often referred to in the literature as EHDP or disodium EHDP, is a white powder, highly soluble in water, with a molecular weight of 250.

Excipients; Magnesium stearate, maize starch, microcrystalline cellulose and starch

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