Patients have rarely reported allergic and skin reactions. Contact your doctor if you develop any symptoms of an allergic reaction including skin rash (with or without blisters), hives, wheezing, or swelling of the face, lips, tongue or throat. Seek immediate medical care if you have trouble breathing, swallowing or feel light-headed.
Patients treated with bisphosphonates have rarely reported serious jaw problems associated with delayed healing and infection, often following dental procedures such as tooth extraction. If you experience jaw problems, contact your doctor and dentist.

GUIDE TO UNDERSTAND POSTMENOPAUSAL OSTEOPOROSIS AND ITS TREATMENT

Your doctor has prescribed you ADROMUX® for the treatment of the bone loss that generally occurs after menopause.
This guide will help you to understand what osteoporosis is and will give you some useful instructions to obtain better results with this treatment.
Keep this leaflet together with you Package and do not hesitate to consult your doctor if you need further information.

WHAT IS OSTEOPOROSIS?

Osteoporosis is a silent disease that may produce no symptoms during many years. It is caused by the loss of bone components, leading to a slow but progressive increase of bone fragility that may result in bone fractures, either spontaneously or as a consequence of minimal traumatism. The most common fractures associated with osteoporosis occur at the hip, spine and wrist.
The accumulation of vertebral cracks over time will cause loss of height and may distort the normal curvature of the spine.
Though osteoporosis is 4-times more frequent in women, it can also affect men.

POSTMENOPAUSAL OSTEOPOROSIS

It is currently known that bones undergo continuous turnover. Over the years, the bone is almost totally renewed by removal of old or waste material (bone resorption) and replacement with newly formed bone (bone formation). These two coupled-mechanisms allow the skeleton to adapt to the requirements and activities of each individual.
During the first stages of human growth and development, the amount of newly formed bone is greater than the amount of removed bone tissue. Bone reaches its maximum density and strength in the second decade of life (20-25 years of age) and from then on and until the age of 40, the amount of new bone formation approximately balances the amount of bone destruction in healthy subjects. After that age, especially during menopause when the ovaries cease estrogen production, the balance shifts to favor bone resorption which can result in debilitating diseases such as osteoporosis. Consequently, as from menopause, the material that builds up bone becomes less dense and more fragile. This process is slow and asymptomatic, until fractures or cracks occur.
One out of 4 postmenopausal women is at risk of fracture.
Loss and progressive deterioration of bone may be prevented, as well as treated if osteoporosis has already been established. Adequate intervention measurements may help recover bone strength and halt the progression of the disease.

WHICH OTHER LIFESTYLE CHANGES MAY BE FAVORABLE?

Physical exercise has a favorable influence on bone quality. It is advisable to avoid sedentary life, make regularly walks (at least 1 hour daily) and practice physical exercise. If possible, sit, stand or run with your back upright. Avoid falls and strikes, and use extra caution when walking on slipping floors, especially in bathrooms and bathtub. Provide adequate illumination to stairways and do not leave toys or small objects on the floor. Do not use unstable or insecure devices to reach high places.
It is advisable to moderate the consumption of meat, salt, alcohol, coffee and tobacco. Drink ¾ liters of milk per day (preferably skim) and eat cheese and yogurt for an adequate calcium supply. Vitamin D is very necessary for calcium metabolism. It is naturally supplied in fish and liver and becomes activated with sunlight exposure; consequently, either moderate sunbathing or walking in the open air during 30 to 60 minutes per day is highly recommended.

FINAL RECOMMENDATION

By following the medical instructions, it is possible to prevent, stop or reverse postmenopausal osteoporosis. The treatment may be prolonged for some years but knowing this may help you fulfill it.
Perseverance is required to experience treatment results, since bones have to undergo their own renewal process.
It is very important that you consult your doctor regularly and you adopt a healthy lifestyle that will allow you to walk upright in the future and help you enjoy your life.

Consult your Doctor

"This medication has been prescribed for your current medical condition. Do not recommend it to other persons".

"KEEP OUT OF THE REACH OF CHILDREN"

ADROMUX®

IBANDRONIC ACID 150 mg

Prescription Only Medicine
Made in Argentina

Coated Tablets

COMPOSITION

Each coated tablet contains:
Ibandronate monosodium monohydrate.....168.750 mg
(equivalent to 150.0 mg of ibandronic acid)
Excipients: Microcrystalline cellulose, pregelatinized starch, Colloidal silicon dioxide, Sodium stearyl fumarate, Croscarmellose Sodium, Opadry YS-1-7003,Opadry YS-7006,Polyetilenglycol 6000.....q.s.

THERAPEUTIC ACTION:

Inhibitor of bone resorption. Antiosteopenic and antiosteoporotic agent.

ATC CODE: M05B A 06

INDICATIONS:

Treatment and prevention of osteoporosis in postmenopausal women.

PHARMACOLOGICAL ACTION:

Ibandronate inhibits osteoclast activity and reduces bone resorption and turnover. Ibandronate action on bone tissue is based on its affinity for hydroxyapatite, which is part of the bone mineral matrix. It reduces the high bone turnover rate in postmenopausal women, thus producing a gain of bone mass.

PHARMACODYNAMIA:

Ibandronic acid induces biochemical changes denoting dose-dependent inhibition of the osteoclast activity, with decreased bone resorption and turnover, evidenced by the decrease of biochemical markers of bone degradation (such as deoxypyridinoline and cross-linked C-telopeptide of Type I collagen), thus leading to a net gain of bone mass, when administered in a once-monthly dose of 150 mg to postmenopausal women.
Treatment with the 2.5 mg daily dose significantly reduces the incidence of new vertebral fractures and increases lumbar spine BMD, in comparison with placebo, when administered concomitantly with calcium and vitamin D supplementation. In a 1-year clinical study comparing once-monthly versus once-daily dosing regimes, the average decrease from baseline values in serum CTX was -76% for patients treated with 150 mg once-monthly and -67% for those treated with 2.5 mg once-daily. After discontinuation of treatment, markers of bone resorption increase again to pretreatment values. Treatment with once-monthly 150 mg of ibandronic acid produces an increase of lumbar spine and hip BMD, which is superior to placebo but not inferior to the once-daily 2.5 mg regime.

PHARMACOKINETICS:

Absorption:

Ibandronate absorption takes place in the upper gastrointestinal tract. Maximum peak concentrations are obtained within a time period from 0.5 to 2 hours (median: 1 hour) following an oral dose in fasted healthy postmenopausal women. Mean oral bioavailability of 2.5 mg ibandronate is approximately 0.6% compared to intravenous administration. Oral bioavailability is reduced by 90% when ibandronate is co-administered with a standard breakfast. However, no bioavailability reduction has been observed when ibandronate is taken at least 60 minutes before breakfast. Consequently, the intake of either food or beverage (other than plain water) reduces ibandronate bioavailability and its effect on bone mineral density.

Distribution:

After absorption, ibandronate is either rapidly taken up by the bone or excreted in the urine. In humans, the volume of distribution is at least 90 liters and the amount of dose removed from circulation by the bone is about 40% to 50%. *In vitro* protein binding in human serum ranges from 99.5% to 90.9% for ibandronate concentrations of 2 to 10 ng/mL, and is approximately 85.7% for concentrations of 0.5 to 10 ng/mL.

Metabolism:

Ibandronate does not undergo hepatic metabolism and does not inhibit the hepatic cytochrome P450 system. Ibandronate is eliminated by renal excretion. There is no evidence that ibandronate is metabolized in humans.

Elimination:

The amount of ibandronate not absorbed into the bone is eliminated unchanged by the kidney (approximately 50% to 60% of the total absorbed dose). Unabsorbed fraction from the gastrointestinal tract is eliminated unchanged in the feces.
Ibandronate elimination from plasma is multiphasic. Its renal clearance and distribution into bone are responsible for a rapid

and early decrease of its plasma concentrations, reaching 10% of the peak plasma concentration (Cmax) within 8 hours after oral administration. Then follows a slower phase during which ibandronate redistributes back into the bloodstream from the bone compartment. The apparent terminal half-life for the 150 mg oral dose ranges from 37 to 157 hours in healthy postmenopausal women.

Total clearance of ibandronate varies from 84 to 160 mL/min. Renal clearance accounts for 50% to 60% of total clearance and is related to creatinine clearance.

Special Populations:

Pediatrics:

Ibandronate pharmacokinetics has not been evaluated in patients below 18 years of age.

Geriatric:

No other differences than age-related changes in renal function have been observed between adult and geriatric patients.

Gender:

Ibandronate bioavailability and pharmacokinetics are similar in both men and women.

Race:

Pharmacokinetic differences among races have not been studied.

Renal impairment:

Renal clearance of ibandronate in patients with renal impairment is linearly related to creatinine clearance (CLcr). After the intravenous administration of a single 0.5 mg ibandronate dose, patients with CLcr 40 to 70 mL/min showed 55% higher exposure (AUC_∞) than the exposure observed in subjects with CLcr >90 mL/min. Patients with CLcr <30 mL/min had more than a two-fold increase in exposure compared to the exposure for healthy subjects.

Liver impairment:

No studies have been performed to assess ibandronate pharmacokinetics in patients with liver impairment because ibandronate is not metabolized in the human liver.

CLINICAL STUDIES

Treatment of postmenopausal women

Daily dosing

A randomized, double-blind, placebo-controlled, multinational study evaluated a total of 2946 postmenopausal women, who had lumbar spine BMD 2 to 5 SD below the premenopausal mean (T-score) and had 1 to 4 prevalent vertebral fractures.

The risk for vertebral fracture was 9.6% in women treated with placebo and 4.7% in patients treated with ibandronic acid 2.5 mg/day.

The histological analysis of iliac crest bone biopsies showed bone of normal quality, without signs of osteomalacia or a mineralization defect.

Once-Monthly Dosing

Another randomized, double-blind, multinational, comparative efficacy trial evaluated 1602 postmenopausal women with L2-L4 lumbar spine BMD T-score below -2.5 SD at baseline. The once-monthly dosing with ibandronate 150 mg showed similar efficacy to the daily ibandronate 2.5 mg dosing, based on lumbar spine BMD values.

Prevention of postmenopausal osteoporosis

Once-Monthly Dosing

In a randomized, double-blind, placebo-controlled one-year study, the once-monthly dose of ibandronate 150 mg prevented bone mass loss in the majority of women (88.2%). This study included 160 postmenopausal women with low bone mass baseline (T-score from -1 to -2.5).

The once-monthly ibandronate 150 mg dose resulted in a mean increase in lumbar spine BMD of 4.12% compared with placebo after 1 year of treatment ($p<0.0001$). BMD at other skeletal sites also increased above baseline values.

DOSAGE AND ADMINISTRATION:

The dosage indicated for the treatment and prevention of postmenopausal osteoporosis is one 150 mg tablet taken once monthly, at regular intervals, most preferably on the same date each month.

- To maximize absorption and clinical benefits, ADROMUX® should be taken at least 60 minutes before the first meal or beverage (other than water) of the day, or before taking any other medication, including antacids, calcium or vitamin supplementation.
- To facilitate delivery to the stomach and thus reduce the potential for esophageal irritation, the tablets should be swallowed whole with a full glass of plain water, while the patient remains standing or sitting upright. Patients should not lie down during the 60 minutes following the intake of ADROMUX®.
- Patients should not eat or drink (except water), or take other medications at least during the 60 minutes following the intake of ADROMUX®.
- Plain water is the only beverage allowed to take ADROMUX®. Mineral water may contain high concentrations of calcium and, hence, should not be used.
- Patients should not chew or suck the tablet because it may cause oropharyngeal ulceration.
- ADROMUX® should be taken on the same date each month (that is, at regular intervals of 30 days).
- Patients should not take 2 ADROMUX® tablets in the same week.
- If the patient forgets to take one monthly dose and there are more than 7 days left before the next scheduled ADROMUX® tablet, then the patient should take one ADROMUX® tablet in the morning following the date that it is remembered. Afterwards, the patient should return to taking the tablet on the day originally scheduled.
- If the patient forgets to take one monthly dose and there are less than 7 days left before the next scheduled ADROMUX® tablet, then the patient should wait until the next scheduled ADROMUX® tablet. Afterwards, the patient should return to taking the tablet on the day originally scheduled.

CONTRAINDICATIONS:

Hypersensitivity to ibandronate or any of ADROMUX® ingredients. Hypocalcemia. Inability to remain standing or sitting upright for at least 60 minutes.

WARNINGS:

Like other orally administered bisphosphonates, ibandronate may cause upper gastrointestinal disorders such as dysphagia, esophagitis, and esophageal or gastric ulcer.

PRECAUTIONS:

General:

An adequate intake of calcium and vitamin D is important in all patients. Patients should receive calcium and vitamin D supplementation if the dietary supply is inadequate. No dose adjustment is required in elderly subject or for patients with liver impairment. No dose adjustment is necessary for patients with mild or moderate renal impairment. The use of ibandronate is not recommended in patients with severe renal impairment (creatinine clearance of <30 mL/min).

Mineral Metabolism

Hypocalcemia and other disturbances of bone and mineral metabolism should be treated before starting ibandronate therapy. An adequate intake of calcium and vitamin D is important in all patients to prevent hypocalcemia. There have been postmarketing reports of hypocalcemia following dosing.

Gastrointestinal disorders:

Orally administered bisphosphonates are associated with upper gastrointestinal disorders such as esophagitis, dysphagia, and esophageal or gastric ulcers. The patients should be instructed to comply with dosing instructions in order to minimize the risk of these effects, and to discontinue the treatment and seek medical attention if any of the following symptoms appear or worsen: esophageal irritation, pain when swallowing, retrosternal pain or heartburn.

Renal impairment:

Ibandronate use is not recommended in patients with severe renal impairment (creatinine clearance <30 mL/min).

Jaw Osteonecrosis:

Cases of osteonecrosis, mainly of the jaw, have been reported in patients treated with bisphosphonates by intravenous route, especially in cancer patients undergoing dental procedures, though some have occurred in orally treated patients due to postmenopausal osteoporosis or other diagnoses. Known risk factors for osteonecrosis include a diagnosis of cancer, concomitant therapies (e.g., corticosteroids, chemotherapy, radiotherapy), and co-morbid disorders (e.g., anemia, coagulopathy, infections, pre-existing dental disease).

For patients who develop osteonecrosis of the jaw during the course of the bisphosphonate therapy, dental surgery may exacerbate the condition. There are no data available to suggest whether the discontinuation of the bisphosphonate treatment may reduce the risk of osteonecrosis of the jaw. The treating physician/dentist should decide on the best treatment option for each patient based on individual benefit/risk assessment.

Musculoskeletal pain:

Severe and occasionally incapacitating bone, joint, and/or muscle pain has been reported in patients treated with bisphosphonates approved for the prevention and treatment of osteoporosis, including ibandronate. However, reports are infrequent and, in the majority of cases, pain ceases after discontinuation of treatment. A subgroup recurred when rechallenged with the same drug or another bisphosphonate. Discontinuation of treatment should be evaluated if severe symptoms develop. Most of patients were postmenopausal women. The time to onset of symptoms varied from one day to several months after starting the drug. In placebo-controlled clinical trials with ibandronate, the amount of patients with these symptoms was similar in both groups.

INTERACTIONS:

Drug interactions

Ibandronate does not inhibit the hepatic cytochrome P450 system and does not appear to compete with transport systems involved in the renal excretion of other drugs.

Products containing any of the following compounds may interact with ibandronate:

- Antacids, calcium supplements or products containing multivalent cations (such as aluminum, magnesium, iron) are likely to interfere with ibandronate absorption and, therefore, should be taken at least 60 minutes after ibandronate oral administration. In addition, patients should wait at least 60 minutes after ibandronate intake in order to take any other oral medication.
- Aspirin and other nonsteroidal anti-inflammatory drugs (NSAIDs): these compounds may cause gastrointestinal irritation and, hence, caution should be taken in case of requiring the concomitant use of these compounds with ibandronate.
- Histamine H2-receptor antagonists: in pharmacokinetic interaction studies in healthy volunteers, co-administration with ranitidine produced a 20% increase in the bioavailability of oral ibandronate, which was not considered to be clinically relevant.

Drug/Laboratory test interactions:

- Bisphosphonates are known to interfere with the use of bone-imaging agents.

CARCINOGENESIS, MUTAGENESIS AND REPRODUCTIVE TOXICITY:

Carcinogenesis

No significant increase of tumor incidence was observed in male and female rats in a 104-week carcinogenicity study, with oral doses (administered by gavage) that produced cumulative exposure up to 3,5 and 2 times higher, respectively, than the human exposure at the recommended once-monthly oral dose of 150 mg.

No significant drug-related tumor findings were observed in a 78-week carcinogenicity study in male and female NMRI mice, with oral gavage doses inducing cumulative exposures up to 135 and 20 times higher, respectively, than the human exposure at the recommended once-monthly oral dose of 150 mg.

In a 90-week carcinogenicity study in male and female NMRI mice, with oral doses administered in the drinking water that produce cumulative monthly exposures up to 70 and 115 times higher, respectively, than the human exposure at the recommended dose of 150 mg, a dose-related increased incidence of adrenal subcapsular adenoma/carcinoma was observed in female mice, which was statistically significant at 60 mg/kg/day (115 times higher than the human exposure at the recommended once-monthly oral dose of 150 mg). The relevance of these findings to humans is unknown.

Mutagenesis

No evidence for a mutagenic or clastogenic potential of ibandronate was observed in *in vitro* bacterial mutagenesis assays (Ames test), mammalian cell mutagenesis assay in Chinese hamster V79 cells, and chromosomal aberration test in human peripheral lymphocytes, each with and without metabolic activation. Ibandronate was not genotoxic in the in vivo mouse micronucleus tests for chromosomal damage.

Reproductive toxicity

No signs of teratogenesis, fetal toxicity or first-generation effects were observed in rats and rabbits treated with oral ibandronate. Reproductive toxicology observed in experimental animals was similar to that observed with other bisphosphonates and included interference with natural parturition and fertility impairment. In female rats treated with oral doses equivalent to 13 times the human exposure at the recommended once-monthly oral dose of 150 mg, decreases in fertility, the number of corpora lutea and implantation sites were observed. In female rats given high oral doses, maternal deaths at the time of delivery were observed in all dose groups. Perinatal pup loss in dams was likely related to maternal dystocia. A low incidence of postimplantation loss was observed in rats treated from 14 days before mating throughout lactation or during gestation, only at doses causing maternal dystocia and periparturient mortality. Periparturient mortality has also been observed with other bisphosphonates, which appears to be a class effect related to inhibition of skeletal calcium mobilization leading to hypocalcemia and dystocia.

Exposure of pregnant rats during the period of organogenesis resulted in an increased fetal incidence of RPU (renal pelvis ureter) syndrome at high oral doses ≥10 mg/kg/day. Impaired pup neuromuscular development (cliff avoidance test) was also observed.

In pregnant rabbits treated with very high oral doses during gestation, dose-related maternal mortality was observed in all treatment groups, which was associated with lung edema and hemorrhage. No significant fetal anomalies were observed.

Pregnancy: Category C

Bisphosphonates are incorporated into the bone matrix, from where they are gradually released over periods of weeks to years. The extent of bisphosphonate incorporation into adult bone, and hence, the amount available for release back into the systemic circulation, is directly related to the total dose and duration of bisphosphonate use. Although there are no data about fetal risk in humans, bisphosphonates cause fetal harm in animals, and animal data suggest that uptake of bisphosphonates into fetal bone is greater than into maternal bone. Therefore, there is a theoretical risk of fetal harm (in the skeletal and other abnormalities) 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 fetal risk has not been established.

No adequate and well controlled studies have been performed in pregnant women. Ibandronate should not be used during pregnancy unless the potential benefit justifies the potential risk to the mother and fetus.

Lactancy

It is unknown whether ibandronate is excreted in human milk. Because many drugs are excreted in human milk, caution should be taken when ibandronate is administered to nursing women. In lactating rats, ibandronate was detected in breast milk. Ibandronate mean concentration in milk was 1.5 times higher than its concentration in plasma.

Pediatric Use

Effectiveness and safety have not been established in children.

ADVERSE REACTIONS:

Once-monthly dosing:

In a two-year comparative study between ibandronate 2.5 mg daily and ibandronate 150 mg once-monthly, in postmenopausal women, safety and tolerability profiles were similar in both oral dosing groups. Patients with active or significant pre-existing gastrointestinal disease were excluded from this trial. Patients with dyspepsia or concomitant use of nonsteroidal anti-inflammatory drugs, proton pump inhibitors and histamine (H_2) antagonists were included in this study.

After one year, the incidence of all-cause mortality was 0.3% in both the ibandronate 2.5 mg daily group and the ibandronate 150 mg once-monthly group. The incidence of serious adverse events was 5% in the ibandronate 2.5 mg daily group and 7% in the ibandronate 150 mg once-monthly group. The percentage of patients who withdrew from treatment due to adverse events was 9% in the 2.5 mg daily group and 8% in 150 mg once-monthly group.

Table: Adverse events with an incidence ≥2% in patients treated with ibandronic acid 2.5 mg daily or 150 mg once-monthly for the treatment of postmenopausal women.

Adverse Reactions	Ibandronic acid 2,5 mg daily % (n=395)	Ibandronic acid 150 mg once-monthly % (n=396)
Vascular Disorders		
Hypertension	7,3	6,3
Gastrointestinal Disorders		
Dyspepsia	7,1	5,6
Nausea	4,8	5,1
Diarrhea	4,1	5,1
Constipation	2,5	4,0
Abdominal Pain[a]	5,3	7,8
Musculoskeletal and Connective Tissue Disorders		
Arthralgia	3,5	5,6
Back Pain	4,3	4,5
Pain in Extremity	1,3	4,0
Localized Osteoarthritis	1,3	3,0
Myalgia	0,8	2,0
Muscle Cramps	2,0	1,8
Infections and Infestations		
Influenza	3,8	4,0
Nasopharyngitis	4,3	3,5
Bronchitis	3,5	2,5
Urinary Tract Infection	1,8	2,3
Upper Respiratory Tract Infection	2,0	2,0
Nervous System Disorders		
Headache	4,1	3,3
Dizziness	1,0	2,3
General Disorders and Administration Site Conditions		
Influenza-like illness[b]	0,8	3,3
Skin and Subcutaneous Tissue Disorders		
Rash[c]	1,3	2,3
Psychiatric Disorders		
Insomnia	0,8	2,0

a Combination of abdominal pain and upper abdominal pain
b Combination of influenza-like symptoms and acute phase reaction
c Combination of rash pruritic, rash macular, rash papular, rash generalized, rash erythematous, dermatitis, dermatitis allergic, dermatitis medicamentosa, erythema and exanthem

Ocular adverse events

Reports in the medical literature indicate that bisphosphonates may be associated with ocular inflammation such as iritis and scleritis. In some cases, these events did not resolve until discontinuation of the bisphosphonate therapy.

Two patients treated with ibandronate 150 mg once-monthly experienced ocular inflammation, one was a case of uveitis and the other scleritis.

Gastrointestinal adverse events

The incidence of adverse events in the groups treated with ibandronate 2.5 mg daily and ibandronate 150 mg once-monthly were, respectively: dyspepsia (7% vs. 6%), diarrhea (4% vs. 5%), and abdominal pain (5% vs. 8%).

Musculoskeletal adverse events

The incidence of adverse events in the groups treated with ibandronate 2.5 mg daily and ibandronate 150 mg once-monthly were, respectively: back pain (4% vs. 5%), arthralgia (4% vs. 6%) and myalgia (1% vs. 2%).

General adverse events and Acute Phase Reactions

Symptoms consistent with acute phase reactions have been reported with the use of different bisphosphonates. Over the two years of the study, the overall incidence of acute phase reaction symptoms was 3% in the ibandronate 2.5 mg daily group and 9% in the ibandronate 150 mg monthly group. These incidence rates are based on the reporting of any of 33

acute-phase reaction like symptoms within 3 days of the monthly dosing and lasting 7 days or less. No patient from the i bandronate 2.5 mg daily group and 2% of the ibandronate 150 mg once-monthly group reported the occurrence of influenza-like illness episodes.
One hundred and sixty (160) postmenopausal women without osteoporosis participated in a 1-year, double-blind, placebo-controlled study with the 150 mg once-monthly dose of ibandronate for the prevention of bone loss. Seventy-seven women received ibandronic acid and 83 subjects received placebo. The overall pattern of adverse events was similar to that previously observed.
After approval of the formulation, some adverse reactions have been reported. Considering that these reactions are reported voluntarily by a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure. Post-approval reports comprise allergic reactions including anaphylaxis, angioedema, bronchospasm and rash; hypocalcemia; bone, joint, or muscle pain (musculoskeletal pain) that is severe or incapacitating; osteonecrosis of the jaw.
Laboratory findings:
A decrease in total alkaline phosphatase levels was observed in ibandronate treated groups compared to placebo, which is consistent with the proper pharmacodynamic action of bisphosphonates. There was no difference compared with placebo for laboratory abnormalities indicative of hepatic dysfunction, hypocalcemia, or hypophosphatemia.

OVERDOSAGE AND TREATMENT:
It may produce dyspepsia, esophagitis, gastritis, hypocalcemia, hypophosphatemia, gastroesophageal ulcer and upset stomach.
There is no specific antidote for ibandronate. Treatment should be symptomatic and supportive. Milk or antacids should be given to bind ibandronate. Due to the risk of esophageal irritation, vomiting should not be induced, and the patient should remain fully upright. Dialysis would not be beneficial.

In case of overdose, go to the nearest Hospital or call Toxicology Center.

How supplied:
Packages containing 1coated tablets.
Storage conditions:
Keep tablets in their original package, at room temperature (between 15 and 30°C).

"KEEP THIS MEDICATION OUT OF THE REACH OF CHILDREN"

GADOR S.A.
Darwin 429 - C1414CUI, Buenos Aires - Phone: (54 11) 4858-9000
Technical Director: Olga N. Greco – Pharmacist
Medicinal product authorized by the Ministry of Health
Certificate N° 53880. Lebanon Reg. N°

Date of Last Revision: 06/2007.

PATIENT INFORMATION

General
Patients should be instructed to read the Patient Information Leaflet carefully before starting ibandronate treatment and to re-read it each time the prescription is renewed.
Patients should be instructed to take calcium and vitamin D supplementation if the dietary supply is inadequate. Moreover, patients should be encouraged to practice weight-bearing exercise and make healthy life-style changes, such as reduction of excessive tobacco and/or alcohol consumption.
Dosing instructions
The recommended regimen for the treatment and prevention of postmenopausal osteoporosis is one tablet of 150 mg once-monthly, taken at regular intervals, preferably on the same date each month.
Remember:
- To maximize absorption and clinical benefits, ADROMUX® should be taken at least 60 minutes before the first meal or beverage (other than water) of the day, or before taking any other medication, including antacids, calcium or vitamin supplementation.
- To facilitate delivery to the stomach and thus reduce the potential for esophageal irritation, the tablets should be swallowed whole with a full glass of plain water, while the patient remains standing or sitting upright. Patients should not lie down during the 60 minutes following the intake of ADROMUX®.
- Patients should not eat or drink (except water), or take other medications at least during the 60 minutes following the intake of ADROMUX®.
- Plain water is the only beverage allowed to take ADROMUX®. Mineral water may contain high concentrations of calcium and, hence, should not be used.
- Patients should not chew or suck the tablet because it may cause oropharyngeal ulceration.
- ADROMUX® tablet should be taken on the same date each month (that is, at regular intervals of 30 days).
- Patients should not take 2 ADROMUX® tablets in the same week.
- In case of taking an excessive dose of ADROMUX®, take a full glass of milk and immediately call the Toxicology Center or nearest Emergency Unit. Do not try to vomit. Do not lie down.
- If the patient forgets to take one monthly dose and there are more than 7 days left before the next scheduled ADROMUX® tablet, then the patient should take one ADROMUX® tablet in the morning following the date that it is remembered. Afterwards, the patient should return to taking the tablet on the day originally scheduled.
- If the patient forgets to take one monthly dose and there are less than 7 days left before the next scheduled ADROMUX® tablet, then the patient should wait until the next scheduled ADROMUX® tablet. Afterwards, the patient should return to taking the tablet on the day originally scheduled.

Patients should receive calcium and vitamin D supplementation if the dietary supply is inadequate. Supplements should be taken at least 60 minutes after the oral administration of ADROMUX® in order to maximize its absorption.
Signs or symptoms indicative of possible esophageal reaction should be carefully monitored by the physician throughout the therapy, and patients should be instructed to interrupt ADROMUX® treatment and seek medical attention if they develop symptoms of esophageal irritation such as pain on swallowing, retrosternal pain, new or worsening dysphagia, or heartburn.
Which are the possible side effects of ADROMUX®?
Discontinue ADROMUX® treatment and seek medical care if you feel:
- Severe heartburn that does not improve.
- Pain or trouble with swallowing
- Chest pain

ADROMUX® may cause:
- Heartburn and retrosternal burning (esophagitis)
- Ulcers in your stomach or esophagus (the tube that connects your mouth and stomach)
- Pain or trouble on swallowing (dysphagia)

The most common side effects observed with ibandronate are:
- diarrhea
- dyspepsia (stomach upset)
- pain in the extremities (arms or legs)

Less common side effects are short-lasting mild flu-like symptoms (which usually improve after the first dose). These are not all the possible side effects of ibandronate.
Patients have rarely reported severe bone, joint, and/or muscle pain after starting the oral treatment with bisphosphonates, which are drugs to treat osteoporosis (thin bones). This group of drugs includes ibandronate. Most patients experienced relief after stopping the drug. Contact your doctor if you develop these symptoms after starting ADROMUX®.