Ibandro®

(Ibandronic Acid)

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Composition
Each film-coated tablet contains 150 mg ibandronic acid (as ibandronate sodium monohydrate).
(PharmEvo Specs.)

Indications
Treatment of osteoporosis in postmenopausal women at increased risk of fracture.
A reduction in the risk of vertebral fractures has been demonstrated, efficacy on femoral neck fractures has not been established.

Adult Dosage
Posology

The recommended dose is one 150 mg film-coated tablet once a month. The tablet should preferably be taken on the same date each month.
ibandronic acid should be taken after an overnight fast (at least 6 hours) and 1 hour before the first food or drink (other than water) of the day or any other oral medicinal products or supplementation (including calcium).

In case a dose is missed, patients should be instructed to take one ibandronic acid 150 mg tablet in the morning after the tablet is remembered, unless the time to the next scheduled dose is within 7 days. Patients should then return to taking their dose once a month on their originally scheduled date.
If the next scheduled dose is within 7 days, patients should wait until their next dose and then continue taking one tablet once a month as originally scheduled.
Patients should not take two tablets within the same week.
Patients should receive supplemental calcium and / or vitamin D if dietary intake is inadequate.

Special Populations:

Patients with renal impairment
No dose adjustment is necessary for patients with mild or moderate renal impairment where creatinine clearance is equal or greater than 30 ml/min.
ibandronic acid is not recommended for patients with a creatinine clearance below 30 ml/min due to limited clinical experience.

Patients with hepatic impairment
No dose adjustment is required.

Paediatric Population
There is no relevant use of ibandronic acid in children.

Method of Administration
For oral use:
Tablets should be swallowed whole with a glass of plain water (180 to 240 ml) while the patient is sitting or standing in an upright position. Patients should not lie down for 1 hour after taking ibandronic acid.
Plain water is the only drink that should be taken with ibandronic acid. Please note that some mineral waters may have a higher concentration of calcium and therefore, should not be used.
Patients should not chew or suck the tablet, because of a potential for oropharyngeal ulceration.

Child Dosage
ibandronic acid has not been tested in these age groups and should not be given to them.

Elderly Dosage
No dosage adjustment is required.

Contra Indications
- Hypocalcaemia
- Hypersensitivity to ibandronic acid or to any of the excipients.

Special Precautions
Gastrointestinal Disorders
Bisphosphonates have been associated with dysphagia, oesophagitis and oesophageal or gastric ulcers. Therefore patients, especially those with a history of prolonged oesophageal transit time, should pay particular attention to and be able to comply with the dosing instructions.

Physicians should be alert to signs or symptoms signalling a possible oesophageal reaction during therapy, and patients should be instructed to discontinue ibandronic acid and seek medical attention if they develop symptoms of oesophageal irritation such as new or worsening dysphagia, pain on swallowing, retrosternal pain, or heartburn.
Since Nonsteroidal Anti-Inflammatory Drugs and bisphosphonates are both associated with gastrointestinal irritation, caution should be taken during concomitant administration.

Hypocalcaemia:
Existing hypocalcaemia must be corrected before starting ibandronic acid therapy.
Other disturbances of bone and mineral metabolism should also be effectively treated.
Adequate intake of calcium and vitamin D is important in all patients.

Renal impairment:
Due to limited clinical experience, ibandronic acid is not recommended for patients with a creatinine clearance below 30 ml/min.

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 intravenously administered bisphosphonates. Many of these patients were also receiving chemotherapy and corticosteroids. Osteonecrosis of the jaw has also been reported in patients with osteoporosis receiving oral bisphosphonates.
A dental examination with appropriate preventive dentistry should be considered prior to treatment with bisphosphonates 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, 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 judgement of the treating physician should guide the management plan of each patient based on individual benefit/risk assessment.

Galactose intolerance:
Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicinal product.

Interactions
Oral bioavailability of ibandronic acid is generally reduced in the presence of food. In particular, products containing calcium and other multivalent cations (such as aluminium, magnesium, iron), including milk, are likely to interfere with absorption of ibandronic acid, which is consistent with findings in animal studies. Therefore, patients should fast overnight (at least 6 hours) before taking ibandronic acid and continue fasting for 1 hour following intake of ibandronic acid.
Calcium supplements, antacids and some oral medicinal products containing multivalent cations (such as aluminium, magnesium, iron) are likely to interfere with the absorption of ibandronic acid. Therefore, patients should not take other oral medicinal products for at least 6 hours before taking ibandronic acid and for 1 hour following intake of ibandro acid. Metabolic interactions are not considered likely, since ibandronic acid does not inhibit the major human hepatic P450 isoenzymes and has been shown not to induce the hepatic cytochrome P450 system in rats. Furthermore, plasma protein binding is approximately 85 % - 87 % (determined in vitro at therapeutic concentrations), and thus there is a low potential for interaction with other medicinal products due to displacement. Ibandronic acid is eliminated by renal excretion only and does not undergo any biotransformation. The secretory pathway appears not to include known acidic or basic transport systems involved in the excretion of other active substances.
In a two-year study in postmenopausal women with osteoporosis (BM 16549), the incidence of upper gastrointestinal events in patients concomitantly taking aspirin or NSAIDs was similar in patients taking ibandronic acid 2.5 mg daily or 150 mg once monthly after one and two years.
Over 1500 patients enrolled in study BM 16549 comparing monthly with daily dosing regimens of ibandronic acid, 14 % and 18 % of patients used histamine (H2) blockers or proton pump inhibitors after one and two years, respectively. Among these patients, the incidence of upper gastrointestinal events in the patients treated with ibandronic acid 150 mg once monthly was similar to that in patients treated with ibandronic acid 2.5 mg daily.
Pharmacokinetic interaction studies in postmenopausal women have demonstrated the absence of any interaction potential with tamoxifen or hormone replacement therapy (oestrogen).
No interaction was observed when co-administered with melphalan/prednisolone in patients with multiple myeloma.

Adverse Drug Reactions
The safety of ibandronic acid 2.5 mg daily was evaluated in 1251 patients treated in 4 placebo-controlled clinical studies; 73 % of these patients came from the pivotal three-year treatment study (MF 4411). The overall safety profile of ibandronic acid 2.5 mg daily in all these studies was similar to that of placebo. The overall proportion of patients who experienced an adverse reaction, i.e. adverse event with a possible or probable relationship to trial medication, in the pivotal treatment study (MF 4411) was 19.8 % for ibandronic acid and 17.9 % for placebo.
In a two-year study in postmenopausal women with osteoporosis (BM 16549) the overall safety of ibandronic acid 150 mg once monthly and ibandronic acid 2.5 mg daily was similar. The overall proportion of patients who experienced an adverse reaction, was 22.7 % and 25.0 % for ibandronic acid 150 mg once monthly and 21.5 % and 22.5 % for ibandronic acid 2.5 mg daily after one and two years, respectively. The majority of adverse reactions were mild to moderate in intensity. Most cases did not lead to cessation of therapy.
Table 1 and table 2 list adverse reactions occurring in more than 1 % of patients treated with ibandronic 150 mg monthly or 2.5 mg daily in study BM 16549 and in patients treated with ibandronic acid 2.5 mg daily in study MF 4411. The tables show the adverse reactions in the two studies that occurred with a higher incidence than in patients treated with placebo in study MF 4411. Within each frequency grouping,

undesirable effects are presented in order of decreasing seriousness.
Data at one year from BM 16549 are represented in Table 1 and cumulative data for the two years from BM 16549 are represented in table 2.

Table 1.

	One year data in study BM 16549	One year data in study BM 16549	Three year data in study MF 4411	Three year data in study MF 4411
System Organ Class/ Adverse reaction	Ibandronic acid 150 mg once monthly (N=396) (%)	Ibandronic acid 2.5 mg daily (N=395) (%)	Ibandronic acid 2.5 mg daily (N=977) (%)	Placebo (N=975) (%)
Gastrointestinal system				
Gastro-oesophageal reflux disease	0.5	0.1	0.4	0.1
Diarrhoea	2.5	1.8	1.4	1.0
Dyspepsia	3.5	2.8	2.1	2.9
Nausea	3.3	3.5	1.8	2.3
Flatulence	0.5	1.0	0.4	0.7
Nervous system				
Headache	0.8	1.5	0.8	0.6
General disorders				
Influenza like illness*	3.3	0.3	0.3	0.2
Fatigue	1.0	0.3	0.3	0.4
Musculoskeletal system				
Arthralgia	1.0	0.3	0.4	0.4
Myalgia	1.5	0.3	1.8	0.8
Skin disorders				
Rash	0.8	1.0	1.2	0.7

Transient, Influenza-like symptoms have been reported with Ibandronic acid 150 mg once monthly, typically in association with the first dose. Such symptoms were generally of short duration, mild or moderate in intensity, and resolved during continuing treatment without requiring remedial measures. Influenza-like illness includes events reported as acute phase reaction or symptoms including myalgia, arthralgia, fever, chills, fatigue, nausea, loss of appetite, or bone pain.

Table 2: Cumulative common adverse reactions (>1/100, 1/10) in Phase III osteoporosis studies that were considered by the investigator to be possibly or probably related to treatment - Two year data from study BM 16549 and three year data from placebo-controlled fracture study MF 4411.

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	One year data in study BM 16549	One year data in study BM 16549	Three year data in study MF 4411	Three year data in study MF 4411
System Organ Class/ Adverse reaction	Ibandronic acid 150 mg once monthly (N=396) (%)	Ibandronic acid 2.5 mg daily (N=395) (%)	Ibandronic acid 2.5 mg daily (N=977) (%)	Placebo (N=975) (%)
Gastrointestinal system				
Gastritis	1.0	0.3	0.7	0.5
Gastro-oesophageal reflux disease	0.8	1.0	0.5	1.0
Oesophagitis	0	1.0	0.5	0.4
Diarrhoea	2.5	2.0	1.4	1.0
Abdominal pain	4.0	3.0	2.1	2.9
Dyspepsia	4.0	6.3	4.0	2.7
Nausea	3.0	3.5	1.8	2.3
Nervous system				
Headache	0.8	1.5	0.8	0.6
General disorders				
Influenza like illness*	3.3	0.3	0.2	0.2
Musculoskeletal system				
Muscle cramp	0.5	1.0	0.1	0.4
Musculoskeletal pain	1	0.5	0	0
Arthralgia	1	0.5	0.4	0.4
Myalgia	1.5	0.3	1.8	0.8
Musculoskeletal stiffness	1.0	0	0	0
Skin disorders				
Rash	0.8	1.0	1.2	0.7

Adverse reactions occurring at a frequency of less than or equal to 1 %:

The following list provides information on adverse reactions reported in study MF 4411 occurring more frequently with ibandronic acid 2.5 mg daily than with placebo and study BM 16549 occurring more frequently with Ibandronic acid 150 mg once monthly than with ibandronic acid 2.5 mg daily. Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness:

Uncommon (1/100 – 1/1,000)

Gastro-intestinal Disorders: gastritis, oesophagitis including oesophageal ulcerations or strictures, vomiting, dysphagia
Nervous System Disorders: dizziness
Musculoskeletal and Connective Tissue Disorders: back pain

Rare (1/1,000 – 1/10,000)

Gastro-intestinal Disorders: duodenitis
Immune System Disorders: hypersensitivity reactions
Skin and Subcutaneous Tissue Disorders: angioedema, face oedema, urticaria

Patients with a previous history of gastrointestinal disease including patients with peptic ulcer without recent bleeding or hospitalisation, and patients with dyspepsia or reflux controlled by medication were included in the once monthly treatment study. For these patients, there was no difference in the incidence of upper gastrointestinal adverse events with the 150 mg once monthly regimen compared to the 2.5 mg daily regimen.

Laboratory test findings:

In the pivotal three-year study with ibandronic acid 2.5 mg daily (MF 4411) there was no difference compared with placebo for laboratory abnormalities indicative of hepatic or renal dysfunction, an impaired haematologic system, hypocalcaemia or hypophosphataemia. Similarly, no differences were noted between the groups in study BM 16549 after one and two years.

Post-marketing Experience:

Osteonecrosis of the jaw has been reported in patients treated by bisphosphonates. The majority of the reports refer to cancer patients, but such cases have also been reported in patients treated for osteoporosis. Osteonecrosis of the jaw is generally associated with tooth extraction and / or local infection (including osteomyelitis). Diagnosis of cancer, chemotherapy, radiotherapy, corticosteroids and poor oral hygiene are also deemed as risk factors.

Presentation:
Ibandro150 mg is available in pack of 1X1's

Instructions:

Use as advised by the physician.
Keep all medicines out of the reach of children.
To be sold on the prescription of a registered medical practitioner only.
Protect from light, heat and moisture.
Store below 30° C.
For suspected adverse drug reaction, email us at reports@pharmevo.biz

For more information on our products
call PharmAssist helpline 0800-82222
Monday to Friday 9:00 am to 6:00 pm
or email us at : pharmassist@pharmevo.biz

ہدایات:
ڈاکٹر کی ہدایات کے مطابق استعمال کریں۔
تمام دوائیں بچوں کی پہنچ سے دور رکھیں۔
صرف رجسٹرڈ ڈاکٹر کے نسخے پر ہی فروخت کی جائے۔
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Our dream, a healthier society

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