Ivana® 150mg

Ibandronic acid

Film-coated tablets

RENATA LIMITED

When to take Ivana® :

The dose of Ivana® is one tablet once a month.
Choose one day of the month that will be easy to remember:
- as for example, the same date or the 1st day of each month.

Use the peel-off stickers to mark the dates on your calendar.

Peel-off Stickers as reminder

মনে রাখার জন্য পিল-অফ স্টিকার

Once Monthly Tablet

Once Monthly Tablet

Once Monthly Tablet

Monthly Calendar

Sun	Mon	Tue	Wed	Thu	Fri	Sat
			1	2	3	4
5	Ivana	7	8	9	10	11
12	13	14	15	16	17	18
19	20	21	22	23	24	25
26	27	28	29	30	31	

It’s important to keep taking Ivana® every month on the same date

প্রতি মাসের একই দিনে ইভানা® সেবন করা গুরুত্বপূর্ণ

Index

Ivana® 150mg

Film-coated tablets

Ibandronic acid

Bisphosphonate - Drugs for treatment of bone diseases

1. NAME OF THE MEDICINAL PRODUCT

Ivana®150mg film-coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains 150 mg Ibandronic acid (as ibandronate sodium monohydrate).

3. PHARMACEUTICAL FORM

Film-coated tablet

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of osteoporosis in postmenopausal women, in order to reduce the risk of vertebral fractures.

4.2 Posology and method of administration

For oral use.

The recommended dose is one 150 mg film-coated tablet once a month. The tablet should preferably be taken on the same date of 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 (see section 4.5) or any other oral medicinal products or supplementation (including calcium):

• 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. In case a dose is missed, patients should be instructed to take one Ibandronic acid 150 mg tablet 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 (see section 4.4 and section 4.5).

Patients with renal impairment

No dosage 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 (see section 4.4 and section 5.2).

Patients with hepatic impairment

No dosage adjustment is required (see section 5.2).

Elderly

No dosage adjustment is required (see section 5.2).

Children and adolescents

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

4.3 Contraindications

- Hypocalcaemia (see section 4.4)
- Hypersensitivity to Ibandronic acid or to any of the excipients.

4.4 Special warnings and special precautions for use

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.

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 (see section 4.2).

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 NSAIDS and bisphosphonates are both associated with gastrointestinal irritation, caution should be taken during concomitant administration. Due to limited clinical experience, Ibandronic acid is not recommended for patients with a creatinine clearance below 30 ml/min (see section 4.2 and section 5.2).

4.5 Interaction with other medicinal products and other forms of interaction

Drug-Food 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.

Drug-Drug Interactions

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 Ibandronic acid. 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. In healthy male volunteers and postmenopausal women, intravenous administration of

ranitidine caused an increase in Ibandronic acid bioavailability of about 20 %, probably as a result of reduced gastric acidity. However, since this increase is within the normal variability of the bioavailability of Ibandronic acid, no dosage adjustment is considered necessary when Ibandronic acid is administered with H2- antagonists or other active substances which increase gastric pH.

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 drug concentrations), and thus there is a low potential for drug-drug interaction 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. Of 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.

4.6 Pregnancy and lactation

There are no adequate data from the use of Ibandronic acid in pregnant women. Studies in rats have shown some reproductive toxicity (see section 5.3). The potential risk for humans is unknown. Ibandronic acid should not be used during pregnancy. It is not known whether Ibandronic acid is excreted in human milk. Studies in lactating rats have demonstrated the presence of low levels of Ibandronic acid in the milk following intravenous administration. Ibandronic acid should not be used during lactation.

4.7 Undesirable effects

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 drug reaction, i.e. adverse event with a possible or probable relationship to trial

medication, 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 drug reactions were mild to moderate in intensity. Most cases did not lead to cessation of therapy.

Table 1 and table 2 list adverse drug reactions occurring in more than 1% of patients treated with Ibandronic acid 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 drug reactions in the two studies that occurred with a higher incidence than in patients treated with placebo in study MF 4411.

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: Common adverse drug reactions (>1/100, ≤ 1/10) in phase III osteoporosis studies that were considered by the investigator to be possibly or probably related to treatment - One year data from study BM 16549 and three year data from placebo-controlled fracture study MF 4411

	One year data in study BM 16549		Three year data in study MF 4411	
System Organ Class/ Adverse drug reaction	Ibandronic acid 150 mg once monthly	Ibandronic acid 2.5 mg daily	Ibandronic acid 2.5 mg daily	Placebo
	(N=396) (%)	(N=395) (%)	(N=977) (%)	(N=975) (%)
Gastrointestinal System				
Dyspepsia	3.3	5.8	4.3	2.9
Nausea	3.3	3.5	1.8	2.3
Abdominal pain	3.5	2.8	2.1	2.9
Diarrhoea	2.5	1.8	1.4	1.0
Flatulence	0.5	1.0	0.4	0.7

	One year data in study BM 16549		Three year data in study MF 4411	
System Organ Class/ Adverse drug reaction	Ibandronic acid 150 mg once monthly	Ibandronic acid 2.5 mg daily	Ibandronic acid 2.5 mg daily	Placebo
	(N=396) (%)	(N=395) (%)	(N=977) (%)	(N=975) (%)
Gastro-oesophageal reflux disease	0.5	1.0	0.4	0.1
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				
Myalgia	1.5	0.3	1.8	0.8

	One year data in study BM 16549		Three year data in study MF 4411	
System Organ Class/ Adverse drug reaction	Ibandronic acid 150 mg once monthly	Ibandronic acid 2.5 mg daily	Ibandronic acid 2.5 mg daily	Placebo
	(N=396) (%)	(N=395) (%)	(N=977) (%)	(N=975) (%)
Arthralgia	1.0	0.3	0.4	0.4
Skin disorders				
Rash	0.8	1.0	1.2	0.7

MedDRA version 6.1* 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 drug reactions (>1/100, ≤ 1/10) in Phase III osteoporosisstudies that were considered by the investigator to be possibly or probably related totreatment - Two year data from study BM 16549 and three year data from placebo- controlled fracture study MF 4411

	Two year cumulative data in study BM 16549		Three year data in study MF 4411	
System Organ Class/ Adverse drug 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				
Dyspepsia	4.0	6.3	4.0	2.7
Nausea	3.0	3.5	1.8	2.3
Abdominal pain	4.0	3.0	2.1	2.9
Diarrhoea	2.5	2.0	1.4	1.0

	Two year cumulative data in study BM 16549		Three year data in study MF 4411	
System Organ Class/ Adverse drug reaction	Ibandronic acid 150 mg once monthly	Ibandronic acid 2.5 mg daily	Ibandronic acid 2.5 mg daily	Placebo
	(N=396) (%)	(N=395) (%)	(N=977) (%)	(N=975) (%)
Gastritis	1.0	0.3	0.7	0.5
Gastro-oesophageal reflux disease	0.8	1.0	0.5	0.1
Oesophagitis	0	1.0	0.5	0.4
Nervous system				
Headache	0.8	1.5	0.8	0.6
General disorders				
Influenza like illness*	3.3	0.3	0.3	0.2
Musculoskeletal system				
Myalgia	1.5	0.3	1.8	0.8

	Two year cumulative data in study BM 16549		Three year data in study MF 4411	
System Organ Class/ Adverse drug 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) (%)
Arthralgia	1.0	0.5	0.4	0.4
Muscle cramp	0.5	1.0	0.1	0.4
Musculoskeletal pain	1.0	0.5	0	0
Musculoskeletal stiffness	1.0	0	0	0
Skin disorders				
Rash	1.0	0	0	0

MedDRA version 7.1 * 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.

Adverse drug reactions occurring at a frequency of less than or equal to 1 % .The following list provides information on adverse drug 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:

Uncommon (1/100 – 1/1,000)

Gastro-intestinal Disorders: dysphagia, vomiting, gastritis, oesophagitis including oesophageal ulcerations or strictures.

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 hospitalization, 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.

4.8 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 hematologic system, hypocalcaemia or hypophosphataemia. Similarly, no differences were noted between the groups in study BM 16549 after one and two years.

4.9 Overdose

No specific information is available on the treatment of over dosage with Ibandronic acid. However, based on a knowledge of this class of compounds, oral over-dosage may result in upper gastrointestinal adverse reactions (such as upset stomach, dyspepsia, oesophagitis, gastritis, or ulcer) or hypocalcaemia. Milk or antacids should be given to bind Ibandronic acid, and any adverse reactions treated symptomatically. Owing to the risk of oesophageal irritation, vomiting should not be induced and the patient should remain fully upright.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacodynamic effects

The pharmacodynamic action of Ibandronic acid is inhibition of bone resorption. *In vivo*, Ibandronic acid prevents experimentally induced bone destruction caused by cessation of gonadal function, retinoids, tumours or tumour extracts. In young (fast growing) rats, the endogenous bone resorption is also inhibited, leading to increased normal bone mass compared with untreated animals. Animal models confirm that Ibandronic acid is a highly potent inhibitor of osteoclastic activity. In growing rats, there was no evidence of impaired mineralization even at doses greater than 5,000 times the dose required for osteoporosis treatment.

Both daily and intermittent (with a dose-free interval of 9-10 weeks of Ibandronic acid was confirmed in a clinical trial (MF 4411), in which Ibandronic acid demonstrated anti-fracture efficacy. In animal models Ibandronic acid produced biochemical changes indicative of dose-dependent inhibition of bone resorption, including suppression of urinary biochemical markers of bone collagen degradation (such as deoxypyridinoline, and cross-linked N-telopeptides of type I collagen (NTX)).

In a Phase 1 bioequivalence study conducted in 72 postmenopausal women receiving 150 mg orally every 28 days for a total of four doses, inhibition in serum CTX following the first dose was seen as early as 24 hours post-dose (median inhibition 28 %), with median maximal inhibition (69 %) seen 6 days later. Following the third and fourth dose, the median maximum inhibition 6 days post dose was 74 % with reduction to a median inhibition of 56 % seen 28 days following the fourth dose. With no further dosing, there is a loss of suppression of biochemical markers of bone resorption.

Mechanism of action

Ibandronic acid is a highly potent bisphosphonate belonging to the nitrogen-containing group of bisphosphonates, which act selectively on bone tissue and specifically inhibit osteoclast activity without directly affecting bone formation. It does not interfere with osteoclast recruitment. Ibandronic acid leads to progressive net gains in bone mass and a decreased incidence of fractures through the reduction of elevated bone turnover towards premenopausal levels in postmenopausal women.

Clinical efficacy

Ibandronic acid 150 mg once monthly

Bone mineral density (BMD)

Ibandronic acid 150 mg once monthly was shown to be at least as effective as Ibandronic acid 2.5 mg daily at increasing BMD in a two year, double-blind, multicentre study (BM 16549) of postmenopausal women with osteoporosis (lumbar spine BMD T score below -2.5 SD at baseline). This was demonstrated in both the primary analysis at one year and in the confirmatory analysis at two years endpoint (Table 3).

Table 3: Mean relative change from baseline of lumbar spine, total hip, femoral neck and trochanter BMD after one year (primary analysis) and two years of treatment (Per-Protocol Population) in study BM 16549.

	One year data in study BM 16549		Two year data in study BM 16549	
Mean relative changes from baseline % [95% CI]	2.5 mg daily (N=318) (%)	150 mg once monthly (N=320) (%)	2.5 mg daily (N=294) (%)	150mg once monthly (N=291) (%)
Lumbar spine L2-L4 BMD	3.9 [3.4, 4.3]	4.9 [4.4, 5.3]	5.0 [4.4, 5.5]	6.6 [6.0, 7.1]
Total hip BMD	2.0 [1.7, 2.3]	3.1 [2.8, 3.4]	2.5 [2.1, 2.9]	4.2 [3.8, 4.5]
Femoral neck BMD	1.7 [1.3, 2.1]	2.2 [1.9, 2.6]	1.9 [1.4, 2.4]	3.1 [2.7, 3.6]
Trochanter BMD	3.2 [2.8, 3.7]	4.6 [4.2, 5.1]	4.0 [3.5, 4.5]	6.2 [5.7, 6.7]

Furthermore, Ibandronic acid 150 mg once monthly was proven superior to Ibandronic acid 2.5 mg daily for increases in lumbar spine BMD in a prospectively planned analysis at one year, p=0.002, and at two years, p<0.001.At one year (primary analysis), 91.3% (p=0.005) of patients receiving Ibandronic acid 150 mg once monthly had a lumbar spine BMD increase above or equal to baseline (BMD responders), compared with 84.0% of patients receiving Ibandronic acid 2.5 mg daily. At two years, 93.5 % (p=0.004) and 86.4% of patients receiving Ibandronic acid 150 mg once monthly or Ibandronic acid 2.5 mg daily, respectively, were responders.

For total hip BMD, 90.0% (p<0.001) of patients receiving Ibandronic acid 150 mg once monthly and 76.7% of patients receiving Ibandronic acid 2.5 mg daily had total hip BMD increases above or equal to baseline at one year. At two years 93.4% (p<0.001) of patients receiving Ibandronic acid 150 mg once monthly and 78.4%, of patients receiving Ibandronic acid 2.5 mg daily had total hip BMD increases above or equal to baseline.

When a more stringent criterion is considered, which combines both lumbar spine and total hip BMD, 83.9% (p<0.001) and 65.7% of patients receiving Ibandronic acid 150 mg once monthly or Ibandronic acid 2.5 mg daily, respectively, were responders at one year. At two years, 87.1% (p<0.001) and 70.5%,of patients met this criterion in the 150 mg monthly and 2.5 mg daily arms respectively.

Biochemical markers of bone turn-over

Clinically meaningful reductions in serum CTX levels were observed at all time points measured, i.e. months 3, 6, 12 and 24. After one year (primary analysis) the median relative change from baseline was -76% for Ibandronic acid 150 mg once monthly and -67% for Ibandronic acid 2.5 mg daily. At two years the median relative change was -68% and -62%, in the 150 mg monthly and 2.5 mg daily arms respectively.

At one year, 83.5% (p= 0.006) of patients receiving Ibandronic acid 150 mg once monthly and 73.9% of patients receiving Ibandronic acid 2.5 mg daily were identified as responders (defined as a decrease ≥50 % from baseline). At two years 78.7% (p=0.002) and 65.6% of patients were identified as responders in the 150 mg monthly and 2.5 mg daily arms respectively.

Based on the results of study BM 16549, Ibandronic acid 150 mg once monthly is expected to be at least as effective in preventing fractures as Ibandronic acid 2.5 mg daily.

5.2 Pharmacokinetic properties

The primary pharmacological effects of Ibandronic acid on bone are not directly related to actual plasma concentrations, as demonstrated by various studies in animals and humans.

Absorption

The absorption of Ibandronic acid in the upper gastrointestinal tract is rapid after oral administration and plasma concentrations increase in a dose- proportional manner up to 50 mg oral intake, with greater than dose-proportional increases seen above this dose. Maximum observed plasma concentrations were reached within 0.5 to 2 hours (median 1 hour) in the fasted state and absolute bioavailability was about 0.6 %. The extent of absorption is impaired when taken together with food or beverages (other than plain water). Bioavailability is reduced by about 90 % when Ibandronic acid is administered with a standard breakfast in comparison with bioavailability seen in fasted subjects.

There is no meaningful reduction in bioavailability provided Ibandronic acid is taken 60 minutes before the first food of the day. Both bioavailability and BMD gains are reduced when food or beverage is taken less than 60 minutes after Ibandronic acid is ingested.

Distribution

After initial systemic exposure, Ibandronic acid rapidly binds to bone or is excreted into urine. In humans, the apparent terminal volume of distribution is at least 90 l and the amount of dose reaching the bone is estimated to be 40-50 % of the circulating dose. Protein binding in human plasma is approximately 85 % - 87 % (determined *in vitro* at therapeutic drug concentrations), and thus there is a low potential for drug-drug interaction due to displacement.

Metabolism

There is no evidence that Ibandronic acid is metabolised in animals or humans.

Elimination

The absorbed fraction of Ibandronic acid is removed from the circulation via bone absorption (estimated to be 40-50 % in postmenopausal women) and the remainder is eliminated unchanged by the kidney. The unabsorbed fraction of Ibandronic acid is eliminated unchanged in the faeces.

The range of observed apparent half -lives is broad, the apparent terminal half-life is generally in the range of 10-72 hours. As the values calculated are largely a function of the duration of study, the dose used, and assay

sensitivity, the true terminal half -life is likely to be substantially longer, in common with other bisphosphonates. Early plasma levels fall quickly reaching 10 % of peak values within 3 and 8 hours after intravenous or oral administration respectively.

Total clearance of Ibandronic acid is low with average values in the range 84-160 ml/min. Renal clearance (about 60 mL/min in healthy postmenopausal females) accounts for 50-60 % of total clearance and is related to creatinine clearance. The difference between the apparent total and renal clearances is considered to reflect the uptake by bone.

Pharmacokinetics in special clinical situations

Gender

Bioavailability and pharmacokinetics of Ibandronic acid are similar in men and women.

Race

There is no evidence for any clinically relevant inter-ethnic differences between Asians and Caucasians in Ibandronic acid disposition. There are few data available on patients of African origin.

Patients with renal impairment

Renal clearance of Ibandronic acid in patients with various degrees of renal impairment is linearly related to creatinine clearance.

No dosage adjustment is necessary for patients with mild or moderate renal impairment (CLcr equal or greater than 30 ml/min), as shown in study BM 16549 where the majority of patients had mild to moderate renal impairment.

Subjects with severe renal failure (CLcr less than 30 ml/min) receiving daily oral administration of 10 mg Ibandronic acid for 21 days, had 2-3 fold higher plasma concentrations than subjects with normal renal function and total clearance of Ibandronic acid was 44 ml/min. After intravenous administration of 0.5 mg, total, renal, and non-renal clearances decreased by 67 %, 77 % and 50 %, respectively, in subjects with severe renal failure but there was no reduction in tolerability associated with the increase in exposure. Due to the limited clinical experience, Ibandronic acid is not recommended in patients with severe renal impairment (see section 4.2 and section 4.4) . The pharmacokinetics of Ibandronic acid was not assessed in patients with end-stage renal disease managed by other than hemodialysis. The pharmacokinetics of Ibandronic acid in these patients is unknown, and Ibandronic acid should not be used under these circumstances.

Patients with hepatic impairment

There are no pharmacokinetic data for Ibandronic acid in patients who have hepatic impairment. The liver has no significant role in the clearance of Ibandronic acid which is not metabolised but is cleared by renal excretion and by uptake into bone. Therefore dosage adjustment is not necessary in patients with hepatic impairment.

Elderly

In a multivariate analysis, age was not found to be an independent factor of any of the pharmacokinetic parameters studied. As renal function decreases with age this is the only factor to take into consideration (see renal impairment section).

Children and adolescents

There are no data on the use of Ibandronic acid in these age groups.

5.3 Preclinical safety data

Toxic effects, e.g signs of renal damage, were observed in dogs only at exposures considered sufficiently in excess of the maximum human exposure indicating little relevance to clinical use.

Mutagenicity/Carcinogenicity:

No indication of carcinogenic potential was observed. Tests for genotoxicity revealed no evidence of genetic activity for Ibandronic acid.

Reproductive toxicity:

There was no evidence for a direct foetal toxic or teratogenic effect of Ibandronic acid in orally treated rats and rabbits and there were no adverse effects on the development in F_1 offspring in rats at an extrapolated exposure of at least 35 times above human exposure. Adverse effects of Ibandronic acid in reproductive toxicity studies in the rat were those observed with bisphosphonates as a class. They include a decreased number of implantation sites, interference with natural delivery (dystocia), and an increase in visceral variations (renal pelvis ureter syndrome).

6. PHARMACEUTICAL PARTICULARS

6.1 Incompatibilities : Not applicable.

6.2 Shelf life : 2 years.

6.3 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.4 Nature and contents of container

Ivana® 150 mg film-coated tablets are supplied in blisters (Aluminium/Aluminium) containing 1 tablet.

6.5 Instructions for use and handling

No special requirement

Packs: Ivana® 150 mg tablet: Each box contains one tablet in Alu-Alu blister pack

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ইবানড্রোনিক এসিড

উপাদান ঃ

ইভানা® ১৫০ মি.গ্রা. ট্যাবলেট: প্রতিটি ফিল্ম-কোটেড ট্যাবলেটে রয়েছে ইবানড্রোনেট সোডিয়াম মনোহাইড্রেট যা ১৫০ মি.গ্রা. ইবানড্রোনিক এসিড এর সমতুল্য।

বিবরণ ঃ

অস্টিওপোরোসিস একটি রোগ যেটা হাড়কে দুর্বল করে ফেলে। অস্টিওপোরোসিস পুরুষ এবং মহিলা উভয় ক্ষেত্রে হতে পারে তবে মেনোপজ (৪৫-৫০ বছর বেশী বয়স্ক মহিলাদের মাসিক বন্ধ হয়ে যাওয়া) পরবর্তী মহিলাদের বেশী হয়ে থাকে। অস্টিওপোরোসিসে প্রথমদিকে উপসর্গগুলি দেখা দেয় না। তা সত্ত্বেও অস্টিওপোরোসিসের রোগীদের উচ্চতা কিছুটা কমে যেতে পারে এবং তাদের হাড় বিশেষ করে মেরুদন্ড, হাতের কব্জি, হিপ বোন ভেঙ্গে যেতে পারে। অস্টিওপোরোসিস প্রতিরোধ করা যায় এবং সঠিক ওষুধের মাধ্যমে চিকিৎসা করা যায়।

ইবানড্রোনিক এসিড অস্টিওক্লাস্টের কার্যক্রম প্রতিরোধ করে এবং বোন রিসর্পশন ও টার্নওভার হ্রাস করে। এটি মেনোপজ পরবর্তী মহিলাদের বোন টার্নওভার হার কমিয়ে পর্যায়ক্রমে হাড়ের ওজন বৃদ্ধি করে। ইবানড্রোনেট খাদ্যনালীর উর্ধ্বাংশে শোষিত হওয়ার পর হাড়ের সাথে দ্রুত আবদ্ধ হয় অন্যথায় অপরিবর্তিতভাবে মূত্রের সাথে বেরিয়ে যায়।

নির্দেশনা ঃ

ইভানা® মহিলা এবং পুরুষদের অস্টিওপোরোসিস প্রতিরোধে ও চিকিৎসায় নির্দেশিত।

প্রয়োগমাত্রা ঃ

অস্টিওপোরোসিসের চিকিৎসা এবং প্রতিরোধে প্রতিমাসে একটি ইভানা® ১৫০ মি.গ্রা. ট্যাবলেট সেব্য।

বিশেষক্ষেত্রে প্রয়োগমাত্রা ঃ

যকৃতের রোগীদের ক্ষেত্রে ঃ

প্রয়োগমাত্রায় কোন পরিবর্তন করার প্রয়োজন নেই।

কিডনীর রোগীদের ক্ষেত্রে ঃ

সামান্য থেকে মাঝারি ধরনের কিডনীর সমস্যায় (ক্রিয়েটিনিন ক্লিয়ারেন্স ৩০ মি.লি./মিনিট বা এর বেশী হলে) প্রয়োগমাত্রায় কোন পরিবর্তন করার প্রয়োজন নেই।

বয়স্কদের ক্ষেত্রে ঃ

প্রয়োগমাত্রায় কোন পরিবর্তন করার প্রয়োজন নেই।

প্রয়োগবিধি ঃ

সর্বোচ্চ শোষণ এবং কার্যকারিতার জন্য ইভানা® ১৫০ মি.গ্রা. ট্যাবলেট নির্ধারিত দিনে সকালে ঘুম থেকে উঠে খাদ্য ও অন্য ওষুধ খাওয়ার কমপক্ষে ১ ঘন্টা আগে এক গ্লাস সাধারণ খাবার পানি দিয়ে খেতে হবে। ইভানা® খাওয়ার ১ ঘন্টার মধ্যে শোয়া যাবে না। এ সময়টুকু বসে বা দাঁড়িয়ে বা স্বাভাবিক কাজ করে বা হেঁটে কাটানো যেতে পারে। কোন মাসের ডোজ বাদ পড়লে পরবর্তী ট্যাবলেট খওয়ার দিনটি যদি অন্তত ৭ দিন পরে থাকে তবে মনে পড়ার পরের দিন সকালেই ইভানা® ১৫০ মি.গ্রা. ট্যাবলেট খেতে হবে এবং পরবর্তী ট্যাবলেট নির্ধারিত দিনেই খেতে হবে। কিন্তু পরবর্তী ট্যাবলেট খাওয়ার দিনটি ৭ দিনের মধ্যে হলে, ভুলে যাওয়া ডোজটি না খেয়ে পরবর্তী নির্ধারিত দিনেই ট্যাবলেটটি খেতে হবে। এক সপ্তাহে দুটি ইভানা® ১৫০ মি.গ্রা. ট্যাবলেট খাওয়া যাবে না।

পার্শ্বপ্রতিক্রিয়া ঃ

ইভানা® এর প্রধান পার্শ্বপ্রতিক্রিয়াগুলো হচ্ছে ডিসপেপ্সিয়া, বমি বমি ভাব, ডায়রিয়া, পেটে ব্যথা, পেশীতে ব্যথা, মাথা ব্যথা, মাথা ঝিমঝিম করা।

প্রতিনির্দেশনা ঃ

ইবানড্রোনিক এসিড বা এর যে কোন উপাদানের প্রতি অতিসংবেদনশীল রোগীদের জন্য ইভানা® প্রতিনির্দেশিত।

সাবধানতা ঃ

হাইপোক্যালসেমিয়া এবং হাড় ও খনিজ পদার্থের বিপাকের সমস্যা চিকিৎসা করে ইভানা® থেরাপী শুরু করতে হবে। রোগীদের পর্যাপ্ত পরিমান ক্যালসিয়াম ও ভিটামিন ডি গ্রহণ গুরুত্বপূর্ণ এবং পরিপাকতন্ত্রের পার্শ্বপ্রতিক্রিয়ার ঝুঁকি কমাতে সেবনবিধি মেনে চলতে হবে।

ড্রাগ ইন্টার‍্যাকশন ঃ

ক্যালসিয়াম ও অন্যান্য মাল্টিভ্যালেন্ট ক্যাটায়ন (অ্যালুমিনিয়াম, ম্যাগনেশিয়াম, আয়রন) ইবানড্রোনেটের শোষণ ব্যাহত করায় ইভানা® নেয়ার পর **১** ঘন্টা পরে খাদ্য বা অন্য ওষুধ খেতে হবে।

গর্ভাবস্থায় এবং স্তন্যদানকালে ঃ

গর্ভাবস্থায় এবং স্তন্যদানকালে ইভানা® খাওয়া উচিত নয়।

সংরক্ষণ ঃ

ঠান্ডা এবং শুষ্ক স্থানে ৩০° সে. তাপমাত্রার নীচে সংরক্ষণ করুন।

সকল প্রকার ওষুধ শিশুদের নাগালের বাইরে রাখুন।

সরবরাহ ঃ

ইভানা® ১৫০ মি.গ্রা. ট্যাবলেট: প্রতিটি বাক্সে বয়েছে ১টি ট্যাবলেটের ব্লিস্টার প্যাক।

বিস্তারিত তথ্যের জন্য ইংরেজী অংশ পড়ুন।

Manufactured by

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