The study listed may include approved and non-approved uses, formulations or treatment regimens. The results reported in any single study may not reflect the overall results obtained on studies of a product. Before prescribing any product mentioned in this Register, healthcare professionals should consult prescribing information for the product approved in their country.

Study No: SB-743830/002

Title : An Open-label, Randomized, Replicate, Four-Period Crossover Study in Healthy Post-Menopausal Women to Assess the Bioequivalence of a Single Unit Dose Tablet of 150 mg Ibandronate to 3 x 50 mg Tablets of Ibandronate

Rationale: Ibandronate administered orally at monthly intervals could offer benefits in terms of patient compliance. A Phase 3 clinical trial (BM 16549) was evaluating both 100 mg, and 150 mg doses of ibandronate given once monthly, compared with the 2.5 mg daily regimen. Post-menopausal women were being dosed monthly with either 2 x 50 mg or 3 x 50 mg tablets of ibandronate. In order to make dosing more convenient and encourage compliance, single unit dose tablets of 100 mg and 150 mg are being developed. The purpose of this study was to establish that the single unit dose tablets of 150 mg are bioequivalent with 3 x 50 mg tablets being used in BM 16549.

Phase: I

Study Period: 13 February 2003 to 28 August 2003

Study Design: This was an open-label, randomized, replicate, four-period crossover study in healthy post-menopausal women.

Centres: 4 centers in the US

Indication: Postmenopausal Osteoporosis

Treatment:
A: three 50 mg tablets ibandronate, fasting
B: one 150 mg tablet ibandronate, fasting
Each subject participated in four dosing sessions. Each dose was separated by 4 weeks. Subjects were randomly assigned to one of two treatment sequences, ABAB or BABA. Each subject received Regimen A in two of the four study sessions and Regimen B in the other two study sessions. Pharmacokinetic samples for measurement of blood SB 743830 concentration were performed up to 192 hours post dose in each session. Pharmacokinetic samples for measurement of urine SB 743830 concentrations were collected over a 96-hour period following dose administration. Blood samples were also collected for pharmacodynamic analysis during each dosing session.

Objectives:
1. To demonstrate the bioequivalence of a single 150 mg tablet of ibandronate relative to 3 x 50 mg tablets of ibandronate in post-menopausal women.
2. To assess the safety and tolerability of a single 150 mg tablet and 3 x 50 mg tablets of ibandronate in post-menopausal women.

Statistical Methods: The primary focus of the statistical analysis of the pharmacokinetic data was to demonstrate the bioequivalence of the single unit tablet Regimen B (150 mg) to three separate tablets Regimen A (3 x 50 mg). Point estimates and associated 90% confidence intervals were computed for the ratio of B:A based on a model consistent with the FDA guidelines. Equivalence would be demonstrated when the 90% confidence interval was completely contained within the range 0.80 to 1.25 for AUC, and 0.75 to 1.33 for Cmax of ibandronate.

Study Population: Healthy post-menopausal women were eligible to be enrolled in this study. They must not have had previous treatment with oral bisphosphonates within 6 months of screening, more than 1 month of treatment within one year prior to screening, more than 3 months of treatment within two years prior to screening. They must also not have had previous treatment with an i.v. bisphosphonate at any time or have had any treatment with other drugs affecting bone metabolism within the last 6 months of screening. Subjects must also not have had any disease or disorder known to influence bone metabolism.

Number of Subjects:	**Group A (3 X 50 mg)**	**Group B (150 mg)**
Planned N	60	60
Dosed N	72	71
Completed n (%)	72	71
Total Number Subjects Withdrawn N (%)	3(4)	4(6)
Withdrawn due to Adverse Events n (%)	0(0)	2(3)
Withdrawn due to Lack of Efficacy n (%)	0(0)	0(0)
Withdrawn for Other Reasons n (%)	3(4)	4(6)
Demographics	**Group A & B**	
N (ITT)	72	
Females: Males	72:0	

Mean Age in Years (sd)	63	
BMI Kg/m^2	26	
White n (%)	45	

Pharmacokinetics (PK),pharmacodynamics (PD), PK/PD Endpoints:

The 90% confidence intervals for the ratio of the geometric means for ibandronate AUC(0-∞) and Cmax were completely contained within the equivalence range of 0.80 to 1.25, indicating that the single unit dose tablet of 150 mg ibandronate is bioequivalent to 3 x 50 mg tablets of ibandronate in post-menopausal women. Ibandronate AUC(0-t), tmax, t1/2 and λz values appeared similar for both formulations.

Both treatment regimens of ibandronate decreased serum C-terminal telopeptides of Type-I collagen (CTX), cross-linked N-terminal telopeptides of Type-I collagen (NTX) and osteocalcin to a similar degree, indicating that both formulations had a similar pharmacodynamic efficacy.

Safety results:

All AEs/SAEs occurring after administration of the first dose of study medication, and on or before the final visit were to reported as Adverse Events. All AEs/SAEs were to be recorded irrespective as to whether they were considered drug related.

At each visit/assessment in the period defined above, AEs/SAEs were to be evaluated by the investigator and recorded. AEs/SAEs were to be recorded until completion of the follow-up visit.

Adverse Events:	**Group A**	**Group B**
N (ITT)	72	71
No. subjects with AEs n (%)	55(76)	50(70)
Most Frequent AEs		
Headache	32(44.4)	28(39.4)
Dyspepsia	5(6.9)	10(14.1)
Dizziness	28(38.9)	24(33.8)
Nausea	6(8.3)	4(5.6)
Diarrhoea	6(8.3	3(4.2)
Back pain	6(8.3)	5(7.0)
Pain	6(8.3)	5(7.0)
Nasopharyngitis	9(12.5)	9(12.7)
Pyuria	6(8.3	3(4.2)
Fatigue	5(6.9)	5(7.0

Serious Adverse Events, n (%) [n considered by the investigator to be related, possibly related, or probably related to study medication]:

Serious adverse events **-**includes fatal and non-fatal events	0	0

Publications:
No Publication

Date Updated: 17-Jan-2006