Clinical Study Synopsis for Public Disclosure

This clinical study synopsis is provided in line with **Boehringer Ingelheim's *Policy on Transparency and Publication of Clinical Study Data***.

The synopsis - which is part of the clinical study report - had been prepared in accordance with best practice and applicable legal and regulatory requirements at the time of study completion.

The synopsis may include approved and non-approved uses, doses, formulations, treatment regimens and/or age groups; it has not necessarily been submitted to regulatory authorities.

A synopsis is not intended to provide a comprehensive analysis of all data currently available regarding a particular drug. More current information regarding a drug is available in the approved labeling information which may vary from country to country.

Additional information on this study and the drug concerned may be provided upon request based on **Boehringer Ingelheim's *Policy on Transparency and Publication of Clinical Study Data***.

2. SYNOPSIS

Name of company: Boehringer Ingelheim		**Tabulated Study Report**		**(For National Authority Use only)**
Name of finished product: Mobic®				
Name of active ingredient: meloxicam		**Page:**	**Number:**	
Ref. to Documentation:	**Volume:**	**Page:**	**To**	**Addendum No.:**
Report date: 17 January 2003	**Number:** U03-3092	**Study period (years):** 27 May 2002 - 15 July 2002		

Title of study:	Bioequivalence study of UHAC 62 XX 10 mg tablets compared with 10 mg capsules following single peroral administration in healthy volunteers (An open-label, randomised, two-way crossover study)
Investigator:	[redacted]
Study centre:	[redacted], Japan
Publication (reference):	Not yet published
Clinical phase:	I
Objectives:	To investigate the bioequivalence between 10 mg tablets (test drug) and 10 mg capsules (reference drug) of meloxicam (UHAC 62 XX) in fasted state.
Methodology:	Open-label, randomised, 2-way crossover Washout period: at least 10 days
No. of subjects entered:	
total:	60
each treatment:	Number of subjects (Medication No) — Treatment period 1 2 group A 30 [redacted] Cap Tab. group B 30 [redacted] Tab. Cap.
Diagnosis and main criteria for inclusion:	Healthy male volunteers, Age ≥ 20 and Age ≤ 35 years, BMI ≥ 18.5 and BMI < 25 (Weight (kg) / Height (m)^2)
Test product:	UHAC 62 XX tablet
dose:	10 mg, single dose
mode of admin.	p.o., in fasted state
batch no.:	02013
Duration of treatment:	Single administration
Reference therapy:	UHAC 62 XX capsule (Mobic® capsule)
dose:	10 mg, single dose
mode of admin.:	p o., in fasted state
batch no.:	02014

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Criteria for evaluation:

Efficacy: Pharmacokinetics
- Primary endpoints: C_{max}, $AUC_{0\text{-}60hr}$
- Secondary endpoints: Plasma concentration profile and pharmacokinetic parameters(t_{max}, $t_{1/2}$, $AUC_{0\text{-}\infty}$, $MRT_{0\text{-}\infty}$)

Safety: Medical examination (interviews etc.), physiological examination (blood pressure, pulse rate, ECG), laboratory tests, adverse events
Classification of adverse events
- Adverse events during the capsule treatment period. Onset occurred within 14 days after the administration of the capsule, and before the conclusion of subject participation or the administration of the tablet.
- Adverse events during the tablet treatment period: Onset occurred within 14 days after the administration of the tablet, and before the conclusion of subject participation or the administration of the capsule.

Statistical methods:

ANOVA was performed for log-transformed parameters except for t_{max} including effects accounting for the following sources of variation: 'sequence', 'subjects nested within sequence', 'period', and 'treatment'. The 2-sided 90% CIs were calculated based on the residual error from ANOVA.

The criteria for BE were that the 90% CIs of the difference between the tablet and the capsule for C_{max} and $AUC_{0\text{-}60hr}$ were within the range from 80% to 125%, according to the Japanese BE guideline [G02-0004].

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SUMMARY – CONCLUSIONS:

Efficacy / pharmacokinetics results:

The geometric mean ratio of the test tablet vs capsule in $AUC_{0\text{-}60hr}$ was 101.3%. The 90% confidence interval (CI) was from 98.9 to 103.8%. The geometric mean ratio of the test tablet vs capsule in C_{max} was 106 4%. The 90% CI was from 102.4 to 110.5%. The other parameters tested as reference parameters, $AUC_{0\text{-}\infty}$, $MRT_{0\text{-}\infty}$, $t_{1/2}$ and t_{max} showed no difference between capsule and tablet.

Safety results:

The overall incidence of adverse events during either capsule or tablet treatment periods was 31.7 % (19/60) The incidence during the capsule treatment period was 20.3% (12/59), and that during the tablet treatment period was 15.0% (9/60) Adverse events with an incidence of at least 5% (≥3/60) during either capsule or tablet treatment periods were abdominal pain NOS (capsule: 2 subjects, tablet: 1 subject), diarrhoea NOS (1, 3), pharyngolaryngeal pain (1, 3), blood creatine phosphokinase increased (1, 2), headache NOS (2, 2) and cough (2, 1). All adverse events were mild or moderate, and there were not any severe or serious events in the study. No subjects were discontinued due to adverse events. Adverse events related to the study drugs were observed in 21.7% (13/60) during either capsule or tablet treatment periods. The incidence during the capsule treatment period was 13.6% (8/59), and that during the tablet treatment period was 10.0% (6/60). Regarding laboratory tests and physiological examinations, mild blood creatine phosphokinase increased was observed in 1 subject during the capsule treatment period, and in 2 subjects during the tablet treatment period. All other abnormal findings were mild and observed in only 1 subject in each parameter.

Conclusions:

The 90% CIs of the difference between tablet and capsule for log-transformed $AUC_{0\text{-}60hr}$ and C_{max} were within the BE acceptance range (80 – 125%). Therefore the capsule and the tablet of 10 mg UHAC 62 XX were proven to be bioequivalent. The safety profiles were judged to be good in both capsule and tablet There was no clinically significant difference in safety profiles between capsule and tablet.