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: 12 November 2002	**Number:** U02-3425	**Study period (years):** 22 November 2001 - 26 December 2001		

Title of study:	Preliminary bioequivalence study of UHAC 62 XX tablets compared with a capsule formulation
Investigator:	[redacted]
Study centre:	[redacted] Japan
Publication (reference):	Not yet published
Clinical phase:	I
Objectives:	The preliminary study was performed in order to investigate the relative bioavailability of UHAC 62 XX capsule and two different tablet formulations (TF1 and TF2), and to obtain data for rational design of a subsequent pivotal bioequivalence (BE) study between capsule and tablet formulations.
Methodology:	Open-label, randomised, three-way cross-over Washout period: at least 7 days
No. of subjects entered:	
total:	9
each treatment:	Number of subjects (Medication No.) — Treatment period 1 2 3 group A 3 [redacted] Cap TF1 TF2 group B 3 TF2 Cap TF1 group C 3 TF1 TF2 Cap.
Diagnosis and main criteria for inclusion:	Healthy male volunteers, Age $\geq$ 20 and Age $\leq$ 35 years, BMI $\geq$ 18.5 and BMI $<$ 25 (Weight (kg) / Height (m)^2)
Test product 1:	UHAC 62 XX TF1 tablet
dose:	10 mg, single dose
mode of admin.	p.o., in fasted state
batch no.:	01033
Test product 2:	UHAC 62 XX TF2 tablet
dose:	10 mg, single dose
mode of admin.:	p.o., in fasted state
batch no.:	01034
Duration of treatment:	Single administration

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: 12 November 2002	**Number:** U02-3425	**Study period (years):** 22 November 2001 - 26 December 2001		

Reference therapy:	UHAC 62 XX capsule (Mobic capsule)
dose:	10 mg, single dose
mode of admin.:	p o., in fasted state
batch no.:	01035
Criteria for evaluation:	
Efficacy:	Pharmacokinetics - Primary endpoints: C_{max}, AUC_{0-72hr} - Secondary endpoints: Plasma concentration profile and pharmacokinetic parameters(t_{max}, $t_{1/2}$, $AUC_{0-\infty}$, MRT_{0-t})
Safety:	Medical examination, physiological examination (blood pressure, pulse rate, ECG), laboratory tests, adverse events
Statistical methods:	The statistical model was ANOVA on 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 two-sided 90% CIs were calculated based on the residual error from ANOVA.

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: 12 November 2002	**Number:** U02-3425	**Study period (years):** 22 November 2001 - 26 December 2001		

SUMMARY – CONCLUSIONS:

Efficacy / pharmacokinetics results:

The mean C_{max} and $AUC_{0\text{-}72hr}$ of both tablets were higher than those of the capsule. The geometric mean ratios of C_{max} of TF1 and TF2 to that of the capsule were 118.6% and 116.6%, respectively, and the %CV calculated from the mean square error in ANOVA for the log-transformed parameter was 9.67%. The 90% CIs of TF1 and TF2 were from 109 4% to 128 5% and from 107.6% to 126.4%, respectively. With regard to $AUC_{0\text{-}72hr}$, the geometric mean ratios for TF1 and TF2 were 107.2% and 103.9% and the %CV was 6.25%. The 90% CIs of TF1 and TF2 were from 101.8% to 113.0% and from 98.6% to 109.4%, respectively. $AUC_{0\text{-}\infty}$, $MRT_{0\text{-}t}$, $t_{1/2}$ and t_{max} were evaluated as reference parameters, and they did not show any obvious differences between the capsule and both tablets. The mean values of the primary parameters of TF2 were slightly closer to capsule than those of TF1.

Safety results:

Adverse events were observed in one out of nine subjects The subject [redacted] showed mild alanine aminotransferase increased, mild aspartate aminotransferase increased, mild blood lactate dehydrogenase increased and moderate blood creatine phosphokinase increased at the pre-dose (i.e 7 days after TF1 administration) and 24 hours post dose (i.e. one day after TF2 administration) in the treatment period 3. The investigator judged that all of these findings were not caused by the test drugs but exercise because 100% of CPK isozyme was MM type. All UHAC 62 XX formulations did not induce any drug related adverse events. All other values beyond the normal ranges in laboratory tests and physiological examinations were considered to be physiological changes by the investigators

Conclusions:

The AUC results suggested the bioequivalence between the capsule and each tablet of 10 mg UHAC 62 XX. However, the C_{max} values of the tablet formulations, TF1 and TF2, were higher than that of capsule and the 90% CIs slightly exceeded the BE criteria. The mean values of C_{max} and $AUC_{0\text{-}72hr}$ of TF2 were closer to capsule than those of TF1. All adverse events were unspecific and regarded as not related to the test drugs Therefore, the safety profile was judged as good in all formulations of UHAC 62 XX