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:				
Name of active ingredient: UH-AC 62 XX,meloxicam		**Page:**	**Number:**	
Ref. to Documentation:	**Volume:**	**Page:** to		**Addendum No.:**
Report date: 30 August 2002	**Number:**	**Study period (years):** 11 June - 28 Sept 2001		

Title of study:	An open, randomised, four-way crossover study in healthy volunteers to evaluate the effect of food on the pharmacokinetics of meloxicam after a single p.o. administration of 22.5 mg meloxicam oral suspension and dose-proportionality over a dosage range of 7.5 mg to 22.5 mg
Investigator:	[redacted]
Study centre:	Human Pharmacology Centre, Boehringer Ingelheim Pharma KG, Ingelheim
Publication (reference):	No
Clinical phase:	I
Objectives:	To assess the effect of food on the pharmacokinetics of meloxicam after a single p.o. administration of 22.5 mg meloxicam oral suspension, and to investigate dose-proportionality over the dosage range 7.5 mg to 22.5 mg.
Methodology:	4-way crossover, randomised, open
No. of subjects entered:	
total:	24 subjects, 12 male and 12 female
each treatment:	24
Diagnosis and main criteria for inclusion:	Healthy male and female subjects
Test product:	Meloxicam (UH-AC 62 XX), oral suspension
dose:	7.5 mg meloxicam, fasted (Treatment 1) 15 mg meloxicam , fasted (Treatment 2) 22.5 mg meloxicam, fed (Treatment 3)
mode of admin.:	p.o.
batch no.:	156 511A
Duration of treatment:	Single administration
Reference therapy:	Meloxicam, oral suspension
dose:	22.5 mg meloxicam, fasted (Treatment 4)
mode of admin.:	p.o.
batch no.:	156 511A

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Criteria for evaluation:

Efficacy: Primary endpoints: C_{max}, $AUC_{0-\infty}$,

Secondary endpoints: t_{max}, AUC_{0-tf}, λ_z, $t_{1/2}$, MRT_{tot}, CL/f, V_z/f

Safety: Pulse rate, systolic and diastolic blood pressure, ECG, standard safety laboratory, adverse events

Statistical methods: The dependence of $AUC_{0-\infty}$ and C_{max} (y) on dose (x) was to be assessed by a general regression model of the type y=axb with parameters a and b. Dose proportionality had to be concluded if the 90 % confidence intervals for b are completely included in the interval 0.80 to 1.20. Confidence intervals were to be computed using the appropriate mean square errors obtained from the analysis of variance. Criteria for an effect of food had to be that two-sided 90% CIs for expected median intra-subject (intra-individual) ratios are contained in the range of 80-125% for $AUC_{0-\infty}$ and within 70-143% for C_{max}. The statistical model had to be ANOVA on log transformed parameters including effects for "sequence", "subjects nested within sequences", "period" and "treatment". In addition to the calculation of CIs, the corresponding point estimates for $AUC_{0-\infty}$ and C_{max} were to be provided.

SUMMARY - CONCLUSIONS:

Efficacy results: Meloxicam plasma concentrations were determined by means of a validated HPLC assay (0.025 - 5.0 µg/mL) with UV detection (assay precision within 5.2 %, assay accuracy within ±1.1%) Mean age of the 24 subjects was 33 years, the mean body weight 74.5 kg.

Due to technical deficiencies concerning the conduct of the study (a relevant number of samples between time-points, subjects and/or periods were most likely mixed up) no pharmacokinetic analysis and subsequent statistical evaluation of PK parameters according to the protocol was performed.

Safety results: All tested doses (7.5 mg, 15 mg, 22.5 mg) of meloxicam oral suspension were well tolerated and there was no significant difference with regard to tolerability between fasted and fed condition.

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Conclusions:	An assessment of the formulation with regard to the primary objectives of this trial (dose-proportionality over the dose range 7.5 mg to 22.5 mg and effect of food on the pharmacokinetics of meloxicam following single dose administration of meloxicam oral suspension) was not possible due to major problems concerning the technical conduct of the study. In consequence, the study will be repeated on the basis of the protocol of the current trial.