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 Pharma KG **Name of finished product:**		**Tabulated Study Report**		**(For National Authority Use only)**
Name of active ingredient: UHAC 62 MU (meloxicam)		**Page:**	**Number:**	
Ref. to Documentation:	**Volume:**	**Page:**	**To:**	**Addendum No.:**
Report date: August 2, 1999	**Number:** 107.224	**Study period (years):** April/May 1999		

Title of study:	Influence of a high fat breakfast on the pharmacokinetics of UH-AC 62 MU (rapid release tablet) given as an oral single dose of 7.5 mg in healthy subjects (two-way crossover, randomized, open).
Investigator:	[redacted]
Study centre (s):	Human Pharmacology Centre, Biberach, Germany
Publication (reference):	No
Clinical phase:	I
Objectives:	Influence of a high fat breakfast on the pharmacokinetic profile of the 7.5 mg meloxicam rapid release tablet.
Methodology:	Two-way cross-over, randomized, open
No. of subjects entered:	
total:	8 subjects (4 male, 4 female)
each treatment:	8 subjects (4 male, 4 female)
Diagnosis and main criteria for inclusion:	healthy male and female subjects
Test Product:	meloxicam, rapid release tablet
dose:	12 mg UH-AC 62 MU (= 7.5 mg UH-AC 62 XX)
mode of admin.:	p.o. after a high fat breakfast
batch no.:	B980916
Duration of treatment:	single administration
Reference therapy:	meloxicam, rapid release tablet
dose:	12 mg UH-AC 62 MU (= 7.5 mg UH-AC 62 XX)
mode of admin.:	p.o. after an overnight fast
batch no.:	B980916
Duration of treatment:	single administration
Criteria for evaluation:	
Efficacy:	Primary endpoints: C_{max}, $AUC_{0-\infty}$ Secondary endpoints: t_{max}, AUC_{0-t}, λ_z, $t_{1/2}$, MRT_{tot}, CL/f, V_z/f
Safety:	Routine safety laboratory, adverse events, ECG, physical examination
Statistical methods:	Descriptive statistics including geometric mean 90% confidence intervals for pharmacokinetic parameters

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SUMMARY CONCLUSIONS:

Efficacy results: Not applicable

Pharmakokinetic results:

Meloxicam plasma concentrations were determined by means of a validated HPLC assay (0.02-5.0 µg/mL) with UV detection (assay precision within 5.7%, assay accuracy within ±5.2 %). Mean age of the 8 subjects was 31 years, the mean weight 67 kg (females 59 kg, males 75 kg).

The high fat breakfast (app. 5000KJ, 64 g fat, 37 g protein and 114.5 g carbohydrates) had no relevant influence, as defined by protocol (decrease in C_{max} by ≥ 50%), on the pharmacokinetics of the rapid release tablet ("Quick tablet"). Geometric mean (%gCV) maximum drug plasma concentrations were 837.7 ng/mL (23.2%) and 613.6 ng/mL (14.5%) for the fasted and fed treatment. Almost identical results were obtained for $AUC_{0-\infty}$: 20940 ng.h/mL (26.0%) for fasted subjects and 21120 ng.h/mL (18.2%) for fed subjects. The onset of absorption was as expected delayed after the high fat breakfast, which is reflected by a later t_{max} value: median t_{max} 6h, range 1.5 h to 10 h [fed] vs 2 h, range 1.5 h to 4 h. [fasted].

C_{max} 90% confidence intervals ranged from 67 % to 90 % with a point estimate of 77 %. 90% confidence intervals for AUC ranged from 92 % to 111 % with a point estimate of 101 %.

Female subjects showed not unexpected moderately higher peak plasma concentrations: Geometric mean (female vs male) C_{max} 682.6 ng/mL vs 613.6 ng/mL [fed] and 962.7 ng/mL vs 728.9 ng/mL [fasted]). The same holds true for the respective AUC values: 23630 ng.h/mL vs 18880 ng.h/mL [fed] and 24230 ng.h/mL vs 18100 ng.h/mL [fasted]. An explanation for this is probably the body weight differences between both genders (app. 20%).

Safety results: There were no adverse events, meloxicam was well tolerated.

Conclusions (pharmacokinetics): TABLE 2.1: 1 Results of the non-compartmental evaluation

N=8		Fasted				Fed				90% CI
		gmean	%gCV	amean	%CV	gmean	%gCV	amean	%CV	
C_{max}	[ng/mL]	837.7	23.2	857.2	23.1	647.2	13.9	652.6	13.9	67 – 90
$AUC_{0-\infty}$	[ng*h/mL]	20940	26.0	21590	28.1	21120	18.2	21450	20.2	92 - 111
t_{max}	[h]	2.0#	1.5-4§	2.313	39.9	6.0#	1.5-10§	5.625	62.1	
AUC_{0-tf}	[ng*h/mL]	19640	24.7	20180	26.1	19770	16.3	20010	17.6	
$AUC_{tf-\infty}$	(%)	5.904	31.9	6.171	33.6	6.072	33.1	6.374	36.0	
AUC_{0-24h}	[ng*h/mL]	11140	17.3	11290	18.1	10700	8.1	10730	8.0	
λ_z	[1/h]	0.0300	15.9	0.0303	15.5	0.0318	18.5	0.0322	18.4	
t½	[h]	23.12	15.9	23.38	16.2	21.82	18.5	22.14	18.3	
MRT_{tot}	[h]	32.01	14.5	32.31	14.7	32.85	16.3	33.26	17.8	
CL/f	[mL/min]	5.969	26.0	6.132	23.6	5.917	18.1	5.995	16.1	
Vz/f	[L]	11.94	19.7	12.15	20.2	11.18	16.8	11.31	16.4	

median; § range

Source Data: Appendix 16.3.2 TABLEs 3 to 5

There were no adverse events, meloxicam was well tolerated. In all subjects the global assessment of tolerability was judged as good.