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		**Tabulated Study Report**		**(For National Authority Use only)**
Name of finished product: Not yet determined				
Name of active ingredient: Meloxicam		**Page:**	**Number:**	
Ref. to Documentation:	**Volume:**	**Page:**	**To:**	**Addendum No.:**
Report date: May 21, 1999	**Number:** 107.217	**Study period (years):** 1998		

Title of study:	Pharmacokinetics and tolerability of a single 15 mg meloxicam dose injected intramuscularly compared to a single oral 15 mg meloxicam tablet in healthy subjects. A two-way cross-over, randomized, open study.
Investigator:	[redacted]
Study centre (s):	Human Pharmacology Center, Biberach, Germany
Publication (refer.):	Not yet published
Clinical phase:	I
Objectives:	To investigate the pharmacokinetics and tolerability of an intramuscular 15 mg meloxicam injection in comparison to the 15 mg oral tablet
Methodology:	Two-way cross-over, randomized, open design
No. of subjects entered:	12
total:	12, 6 male and 6 female
each treatment:	12, 6 male and 6 female
Diagnosis and main criteria for inclusion:	Healthy male and female subjects
Test Product:	Meloxicam intramuscular injection
dose:	15 mg UH-AC 62 XX
mode of admin.:	i.m.
batch no.:	708521
Duration of treatment:	Single dose administration
Reference therapy:	Meloxicam tablet
dose:	15 mg UH-AC 62 XX
mode of admin.:	p.o., tablet given after breakfast with 200 ml water
batch no.:	808569
Criteria for evaluation:	
Efficacy:	Primary endpoints: plasma concentration-time course after intramuscular dose, oral pharmacokinetics of meloxicam,
Safety:	Local and systemic tolerability, laboratory findings
Statistical methods:	Descriptive statistics, 90% confidence intervals for test / reference ratio of AUC.

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SUMMARY CONCLUSIONS:

Efficacy results: see pharmacokinetics results

Pharmacokinetic results:

Meloxicam in plasma was measured by an HPLC assay with ultraviolet detection. Quality controls with an assay precision within 4.7% and a deviation from theory within ±10.0 % demonstrated adequate assay performance.

Twelve subjects included in the pharmacokinetic analysis had a mean age of 30.8 (range 22 to 42) years, a mean weight of 71.6 kg (range 59 to 87 kg) and a mean height of 172.9 cm (range 159 to 184 cm).

C_{max} values were reached at app. 1.5 hour after i.m. injection [Test] and at about 6 hours after oral [Reference] administration. Geometric means C_{max} (%gCV) values amounted 1813 (11.0) [Test] vs. 1605 (15.4) [Reference] ng/ml and the respective 90% confidence intervals for C_{max} were in the range of 107% to 120% with a point estimate of 113%.
The geometric mean $AUC_{0-\infty}$ (%gCV) values were also comparable and reached 40443 (29.2) [Test] vs. 43510 (33.3) [Reference] ng·h/ml. The 90% confidence intervals for $AUC_{0-\infty}$ of Meloxicam ranged from 87% to 99% with a point estimate of 93%.

Table 2.1: Results of the noncompartmental pharmacokinetic evaluation (n=12):

		Ampoule 15mg, test				Tablet 15mg, reference			
parameter	unit	gmean	%gCV	mean	%CV	gmean	%gCV	mean	%CV
C_{max}	[ng/ml]	1813	11.0	1823	11.0	1605	15.4	1622	15.6
t_{max}	[h]	#1.25	§0.75-4	1.688	64.2	#6.0	§2-10	6.667	43.1
AUC	[ng·h/ml]	40443	29.2	42002	28.9	43510	33.3	45715	33.7
AUC_{0-t}	[ng·h/ml]	38496	27.7	39825	27.2	41789	30.4	43556	30.8
$AUC_{t-\infty}$	(%)	4.286	53.1	4.788	49.8	3.081	82.23	3.918	71.81
λ_z	[1/h]	0.0384	38.2	0.0411	41.8	0.0402	36.4	0.0425	34.7
$t_{½}$	[h]	18.04	38.2	19.11	32.9	17.23	36.4	18.23	34.5
MRT_{tot}	[h]	24.51	32.8	25.68	32.0	27.20	29.5	28.24	28.3
CL/f	[ml/min]	6.181	29.2	6.412	27.5	5.746	33.3	6.017	30.4
V_z/f	[L]	9.655	19.9	9.823	18.8	8.572	11.4	8.623	11.3

#: median, §: range

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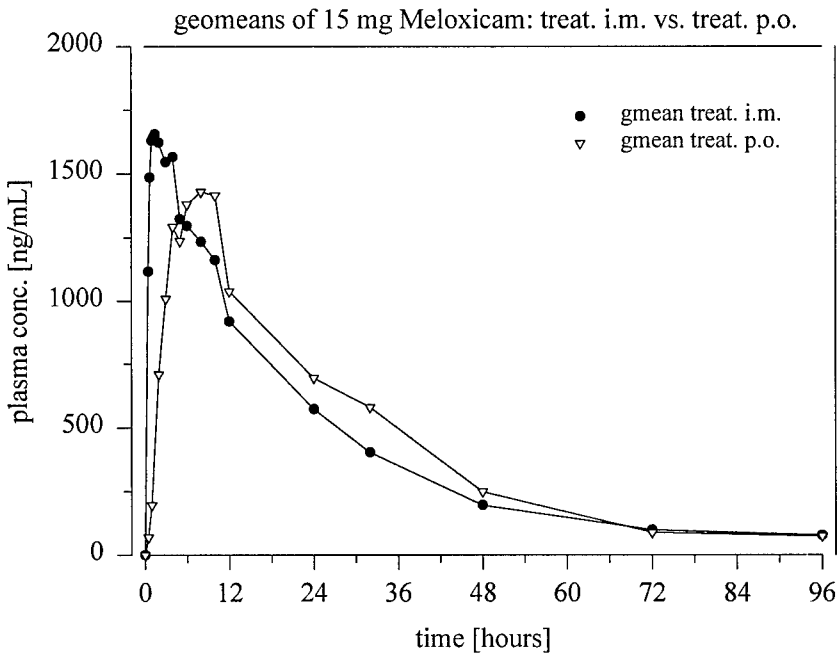
Efficacy results (pharmacokinetics): (continued)

Figure 2:1 Geomeans of 15 mg Meloxicam: Treatment i.m. versus treatment p.o.



Safety results:
Tolerability was rated as good in all cases and in both formulations. The local tolerability was also good, no reddening, swelling, heat or pain on pressure was observed or reported after intramuscularly injected meloxicam. Three of 12 subjects reported a total of 5 adverse events: 2 episodes of functional circulatory disorder (both while taking blood from a forearm vein), 1 episode of herpes labialis, coughing and dysuria. None of the adverse events were related to trial medication. Four episodes were mild or moderate in intensity and a functional circulatory disorder was considered to be severe.
There was no association between treatment group and adverse reaction. Vital signs, ECG and laboratory values did not change compared to baseline.

Conclusions:
Absorption of meloxicam, following an intramuscular injection of 15 mg was significantly faster in comparison to an equal dose applied via the peroral route (tablet). However the extent of absorption was equivalent for both formulations and thus the relative bioavailability of the i.m. application vs. the oral one amounted approximately 93%.
Both treatments were well tolerated.