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: UH-AC 62 XX, Meloxicam Tablets		**Page:**	**Number:**	
Ref. to Documentation:	**Volume:**	**Page:** xxx **to** xxxx		**Addendum No.:** None
Report date: 06 June 2001	**Number:**	**Study period (years):** 04 May 2000 to 15 September 2000		

Title of study:	A double blind, randomized, parallel group trial to compare the effect of three doses of meloxicam tablets (7.5, 15 and 30 mg) with placebo on bleeding time in healthy subjects; with extended-release indomethacin capsules 75 mg (open-label) as an active control to assess trial sensitivity.
Investigator:	[redacted]
Study center(s):	[redacted]
Publication (reference):	
Clinical phase:	IIIb/IV
Objectives:	To study effect of meloxicam (7.5, 15 and 30 mg) with extended-release (ER) indomethacin (75 mg) on bleeding time in healthy subjects
Methodology:	Randomized, placebo-controlled, double-blind, parallel study (indomethacin portion open-label)
No. of subjects entered:	
total:	82 patients
each treatment:	16 patients each in Placebo and meloxicam (15 and 30 mg) and 17 patient each in meloxicam 7.5 mg and indomethacin ER 75 mg.
Diagnosis and main criteria for inclusion:	Healthy male or female subjects, age 18-55 years
Test product:	Meloxicam Tablets
dose:	Three Doses: 7.5 mg, 15 mg, 30 mg
mode of admin.:	Oral
batch no.:	PD-1738
Duration of treatment:	8 days
Reference therapy:	Extended-release Indomethacin capsules or Placebo Meloxicam Tablets
dose:	75 mg / 0 mg
mode of admin.:	Oral / Oral
batch no.:	COC 78 / PD-1741

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Efficacy:	**Primary:**	Bleeding time
	Secondary:	Platelet aggregation, platelet count, platelet thromboxane B_2 synthesis, thromboplastin time, activated partial thromboplastin time, plasma levels of meloxicam and indomethacin. Leukocyte activation
Safety:	Evaluation of adverse events	
Statistical methods:	Analysis of Variance, Analysis of Covariance and Wilcoxon rank sum test and t-test	

SUMMARY – CONCLUSIONS:

Efficacy results:

In this placebo-controlled study the eight-day treatment with meloxicam (7.5 mg, 15 mg, 30 mg) had no detectable effect on bleeding time, the primary efficacy endpoint. Bleeding time was not influenced by meloxicam treatment at any of the three doses examined at anytime point, with pvalues for meloxicam 7.5mg of p=0.79, meloxicam 15 mg of p=0.57 and meloxicam 30 mg of p=0.39, compared to placebo. In contrast, indomethacin ER (75 mg) treatment group, when compared to placebo at the 6 hours post-dose on Day 8, significantly ($p<0.03$) prolonged the bleeding time. Meloxicam treatment also failed to meaningfully influence secondary efficacy endpoints, which included platelet aggregation to adenosine diphosphate (ADP), U46619, arachidonic acid (AA) and collagen. In contrast, in indomethacin ER treated subjects, these variables were affected. In general, there appeared to be no difference in platelet aggregation induced by U46619, between any of the treatment groups. Collagen and platelet aggregation in all three meloxicam treatment groups seemed to be significantly better than in the placebo group at six hours post dose on Day 8. Indomethacin ER significantly inhibited AA at every time point on Day 8 with p values of $p<0.0001$ at each of pre-dose, three hours and six hours post dose. Indomethacin ER also significantly inhibited ADP on Day 8 at three hours and six hours post-dose with p values of 0.03 and 0.04 respectively. This was significant as compared to placebo and all three doses of meloxicam. Thromboxane B2 synthesis was significantly inhibited by all doses of meloxicam and indomethacin compared to placebo at 6 hours post dose on Day 8. This inhibition after meloxicam was dose dependent. Treatment with any of three doses of meloxicam or indomethacin ER showed no meaningful effect on platelet count, prothrombin time (PT) or activated partial thromboplastin time (APTT).

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Safety results:	Eight-day treatment with study drugs (meloxicam, indomethacin ER) was well tolerated and no deaths or serious adverse events were reported. The adverse events most often reported were dizziness, headache and abdominal pain. Six subjects experienced dizziness, one in meloxicam 7.5 mg; one in meloxicam 15 mg; none in meloxicam 30 mg and placebo and four in indomethacin ER 75 mg. Two subjects experienced headache, one in meloxicam 7.5 mg and one indomethacin ER 75 mg, and lastly abdominal pain was reported in two subjects, both of them in indomethacin ER 75 mg treatment group. There was one subject discontinued due to an AE. This subject received indomethacin ER 75 mg and was discontinued due to abdominal pain, dizziness and nausea.
Conclusions:	Meloxicam in conventional and supratherapeutic doses was found to have no effect on bleeding time or platelet aggregation in healthy volunteers, despite dose-related suppression of thromboxane. These results provide further evidence that meloxicam does not have a negative impact on platelet activity and function.