Boehringer Ingelheim

Clinical Study Synopsis for Public Disclosure

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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.

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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**.

Name of company: Boehringer Ingelheim International GmbH		**Tabulated Study Report**	Boehringer Ingelheim
Name of finished product: MOBIC®			
Name of active ingredient: Meloxicam		**Page 1 of 5**	
Report date: 17 APR 2005	**Trial Number:** 107.266	**Study period (dates):** JUL 2004 – DEC 2004	**Date of Revision**

Title of study:	A randomized, open-labelled study to compare the efficacy and safety of meloxicam 15 mg IM ampoules once daily and meloxicam 15 mg tablets administered orally once daily over a period of 7 days in patients in RA.
Investigator:	[redacted]
Study center(s):	Multicentre trial: 7
Publication (reference):	None
Clinical phase:	III
Objectives:	Safety and efficacy of meloxicam 15 mg intra-muscular ampoule once daily compared with meloxicam 15 mg tablets orally once daily over a treatment period of seven days.
Methodology:	Randomised, open-labelled, two groups comparison, multicentre.
No. of subjects:	
total:	150 randomised and treated
each treatment:	75 meloxicam 15 mg intra-muscular, 75 meloxicam 15 mg per os
Diagnosis and main criteria for inclusion:	Archive rheumatoid arthritis (pain rated > 40 mm on a visual analogue scale) after nonsteroidal anti-inflammatory drugs wash-out.
Test product:	Meloxicam ampoules
dose:	15 mg
mode of admin.:	Intra-muscular
batch no.:	326917
Duration of treatment:	Seven days
Reference therapy:	Meloxicam tablets
dose:	15 mg
mode of admin.:	oral
batch no.:	384009

Criteria for evaluation:

Efficacy:

Primary endpoints:

Patient's assessment of overall pain:

Patient's global assessment of disease activity.

Secondary endpoints: Tender joint count, swollen joint count, investigator's global assessment of disease activity, investigator's global assessment of physical function, duration of morning stiffness, patient status with regard to change of arthritic condition, onset of action, time to maximum pain relief, paracetamol consumption, withdrawals due to inadequate efficacy, final global efficacy.

Safety:

Assessment of local tolerability, assessment of overall tolerability, number, nature and severity of adverse events, laboratory investigations, withdrawals due to safety reasons.

Statistical methods:

Intent-to-treat analysis for all parameters:

Efficacy: t-test, Wilcoxon test or Fischer's exact, 95 % confidence intervals for the difference between the treatments, log-rank test.

Safety: Tabulation of adverse events by body System Organ Class, odds ratio, Fischer's exact test, score analysis referring to normal ranges for laboratory parameters.

SUMMARY – CONCLUSIONS:

Efficacy results:

Overall pain assessed by patients.

In ITT set, there was a statistically significant decrease on both treatment groups between baseline values and last value (p = 0.0001). Regarding the reduction from the baseline value, there is statistically significant difference between the two meloxicam formulations (p = 0.044, adjusted by baseline value, and the impact of centres had beed deducted). The mean ± SD of the reduction from baseline in overall pain intensity was – 21.94(18.21)mm in the meloxicam ampoules group and -17.50(16.92) mm in the meloxicam tablets group. The mean ± SD of difference of the reduction between 2 treatment groups is -4.92(-9.72, -0.12)mm. Regarding the predefined equivalence margin of 10mm, the upper limit of mean of difference didn`t exceed the equivalence margin. The conclusion of noninferiority is drawn. The interaction between center and group had been tested. No significant result was found (P>0.1). It is therefore considered that the results from each centers are coincide with each other.

In PP set, there was a statistically significant decrease in both treatment groups between baseline values and last value (p=0.0001). But there is no statistically significant difference between the two meloxicam formulations (p = 0.080, adjusted by baseline value, and the impact of centres had been deducted). The mean ± SD of reduction from baseline in overall pain intensity was -21.62(18.08) mm in the meloxicam ampoules group and -17.71(16.91) mm in the meloxicam tablets group. The mean ± SD of difference of reduction between 2 treatment groups is -4.40(-9.34, 0.53)mm. Regarding the equivalence margin of 10mm, the upper limit of mean of difference didn't reach the equivalence margin. The conclusion of noninferiority is drawn. The interaction between enter and group had been tested. No significant result was found (P>0.1). It is therefore considered that the results from each centres are coincide with each other.

As this clinical trial is designed as a noninferiority study, ITT set and PP set go the same conclusion.

	Disease assessed by the patient: In ITT set, the decrease of VAS were 20.29, 16.64 in ampoules group and tablets group respectively. In ANCOVA model, there is no statistical significant difference between 2 treatment groups after the effect of baseline and center being deducted. The means of reduction from the base line after treatment and their 95 % confidence intervals were -21.65(-25.23, -18.07) and -17.75(-21.25,-14.25) in ampoules group and tablets group respectively. The difference of reduction between 2 treatment group and tablets group respectively. The difference of reduction between 2 treatment groups was -3.90(-8.50,0.70). The result of PP set was conicide with that of ITT.
Safety results:	Both meloxicam routes of administration were safe and well tolerated. 21 patients (24.7 %) in the meloxicam 15 mg ampoules group, and 14 patients (16.3 %) in the meloxicam 15 mg tablets group experienced at least one adverse event (AE). The type and frequency of AEs were similar in both treatment groups (11.76 %) and disorders of the gastrointestinal in meloxicam tablets group (6.98 %). No SAE reported. 3 patients were withdrawn for AE during study, 2 subjects in ampoules group and 1 in tablets group. Overall tolerability was assessed either as good or satisfactory by 80 patients (96 %) in the group treated with meloxicam 15 mg ampoules, and 80 patients (96 %) in the group treated with meloxicam 15 mg tablets. Local tolerability of meloxicam IM injections assessed by the patient and by the investigator was excellent. Assessment of haematological and laboratory parameters did not reveal any significant changes.

Conclusions:	This study confirms that the efficacy of meloxicam 15 mg IM formulation is noninferior to that of meloxicam 15 mg tablets in short term treatment of acute flares of RA. With a trend in favour of the IM formulation in comparison with the PO formulation which reached the threshold of significance for the patient's assessment of physical function, patient status with regard to change of arthritic condition, time to maximum pain relief, final global assessment of efficacy. Both meloxicam 15 mg IM and meloxicam 15 mg tablets were safe and well tolerated, with a comparable severity and incidence of AEs and local tolerability of the meloxicam IM formulation was excellent. It can be concluded, that meloxicam 15 mg ampoules can be considered as a suitable alternative to the tablets during the initial period of treatment of acute flares of RA