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***.

Name of company: Boehringer Ingelheim		**Tabulated Trial Report**	Boehringer Ingelheim
Name of finished product: Mobic®			
Name of active ingredient: Meloxicam		**Page:** 1 of 7	**Synopsis No.:**
Module:		**Volume:**	
Report date: 17 Dec 2008	**Trial No. / U No.:** 107.246 / U08-3888-01	**Date of trial:** 15 Oct 2001 - 30 Sep 2004	**Date of revision** (if applicable)**:**

Title of trial:	Safety and efficacy of meloxicam (MOBIC) compared to other NSAIDs in approved therapeutic dosages and routes of administration in an observational cohort study of patients with Rheumatoid arthritis, Osteoarthritis, Lumbago, Scapulohumerla periarthritis, Neck, shoulder and arm syndrome
Trial sites:	Multicentre study
Publication (reference):	Data of this study has not been published
Clinical phase:	IV
Objectives:	To assess the safety profile of meloxicam by comparing incidence of gastrointestinal adverse events of meloxicam with that of NSAID in the routine daily therapeutic situation.
Methodology:	Open label, observational study
No. of subjects:	
planned:	entered: 9984
actual:	enrolled: 9984 Treatment Meloxicam: entered: 5626 treated: 4358 analysed (for primary endpoint): 5221 Treatment Other NSAIDs: entered: 4358 treated: 5626 analysed (for primary endpoint): 3904
Diagnosis and main criteria for inclusion:	Patients who satisfied all the following criteria were eligible 1. Virgin cases administrated meloxicam/NSAIDs or changed cases from other NSAIDs except etodolac to meloxicam or from meloxicam to other NSAIDs except etodolac 2. Rheumatoid arthritis, Osteoarthritis, Lumbago, Scapulomeral periarthritis, Neck, shoulder and arm syndrome

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Test product:	Meloxicam capsules
dose:	5 mg, 10 mg
mode of admin.:	Po
batch no.:	NA
Reference therapy:	Other NSAIDs
dose:	NA
mode of admin.:	Po
batch no.:	NA
Duration of treatment:	6 months
Criteria for evaluation:	The severity of pain was measured by a five point verbal rating scale (Extremely painful, Acutely painful, Painful, Slightly painful, Pain-free) on visit 1 and final visit
Efficacy / clinical pharmacology:	

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Safety:

Adverse events

Adverse events (AEs) are all complaints of well-being, subjective and objective symptoms (including clinically significant changes of laboratory results), intercurrent diseases and accidents observed during the study.

Adverse drug reactions

Adverse drug reactions (ADRs) are all complaints of well-being, subjective and objective symptoms (including clinically significant changes of laboratory results), intercurrent diseases and accidents observed during the study considered to be drug related.

At each visit, the occurrence and severity of adverse events will be assessed and evaluated.

Serious adverse drug reactions

Serious adverse drug reactions (SADRs) are those events where one or more of the following criteria is fulfilled:

1.fatal

2.disability

3.life threatening

4.hospitalization or prolongation of the period of admission to hospital

5.severe cases corresponding to those 1 to 4

6.a congenital abnormality/medically significant birth defect

Primary endpoint

• Incidence for adverse event of gastrointenstinal disorder

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Secondary endpoint

- Incidence for adverse drug reaction of gastrointestinal disorder
- Incidence of adverse events
- Incidence of adverse drug reactions
- Incidence of serious adverse events
- Incidence for adverse events Perforation, Ulcer and Bleeding (PUB) in the upper gastrointestinal tract

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Statistical methods:

Adverse events will be allocated to LLT and grouped according to system organ classes of MedDRA.

The covariant factor with related occurring adverse event

- Gender
- Age
- Drug (Mobic and other NSAIDs)
- History of adverse drug reaction due to NSAIDs
- Concomitant therapy of DMARD
- Concomitant therapy of ASPIRIN®
- Current disease

1. Rheumatoid arthritis and other disease

2. Rheumatoid arthritis (concomitant therapy with DMARD or Steroid) and other disease

- History of gastrointestinal disorder
- Administration category (Verginal or switched from other NSAIDs)
- Smoking
- Alcohol drinking
- Concomitant therapy with stomach medicine
- Concomitant diagnosis with renal disease
- Concomitant diagnosis with liver disease

Odds ratio and the 95% confidence intervals will be calculated for occurring adverse event by logistic regression with above factors as covariable. For period until initial occurring adverse event hazard ratio and the 95% confidence interval will be calculated by COX regression with same factors. In order to estimate risk factor for occurring adverse event of meloxicam, same analysis as above will be done for meloxicam group

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SUMMARY – CONCLUSIONS:

Efficacy / clinical pharmacology results:

Each patient was classified according to the change from baseline to the end of treatment or Week 24 in the pain grade into three categories: improved, unchanged and worsened. A responder was defined as an improved patient and the efficacy rate was calculated. In 5198 patients in the efficacy analysis set, the efficacy rate was 86.8% (4512/5198). The efficacy rate by indication was similar for osteoarthritis (89.1%), lumbago (90.1%), shoulder periarthritis (89.7%) and cervicobrachial syndrome (90.2%), while that for rheumatoid arthritis (66.3%) was lower as compared to that for the other indications

Safety results:

The numbers of patients surveyed were 5,221 patients treated with Mobic and 3,904 patients treated with other NSAIDs.

The incidences of adverse events involving gastrointestinal disorders without adjustment for the prognostic factors were 3.1% (163 /5221 patients) among those who treated with Mobic and 4.2% (163 /3904 patients) among those who treated with other NSAIDs. The odds ratio for NSAIDs of Mobic adjusted for prognostic factors was 0.64 (95% confidence interval, 0.51-0.81), and the incidence was significantly lower among those who treated with Mobic.

It is calculated an odds ratio and the 95 % confidence interval by logistic analysis for frequency of adverse drug reaction involving gastrointestinal disorders, frequency of adverse event, frequency of adverse drug reaction, frequency of serious adverse event and frequency of adverse event of PUB (Perforation, Ulcer and Bleeding) as secondary endpoints.

The odds ratio for NSAIDs of Mobic adjusted for prognostic factors was 0.64 (95% confidence interval, 0.50-0.80) in adverse drug reaction involving gastrointestinal disorders, 0.70（95% confidence interval, 0.58-0.85) in adverse event, 0.66（95% confidence interval, 0.54-0.81) in adverse drug reaction, 1.29（95% confidence interval, 0.54-3.06) in serious adverse event and 0.80（95% confidence interval, 0.35-1.82) in adverse event of PUB. The incidence of adverse drug reaction involving gastrointestinal disorders, adverse event and adverse drug reaction was significantly lower among those who treated with Mobic. The incidence of serious adverse event and adverse event of PUB was almost equal to NSAIDs.

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Conclusions:	We conducted an observational cohort study using a simultaneous comparison group, within the framework of the current post-marketing surveillance of pharmaceutical products used in routine clinical practice. This survey in routine clinical practice confirmed that, as compared to other NSAIDs, Mobic was associated with significantly fewer adverse events and significantly fewer gastrointestinal disorders.