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: MICARDIS®				
Name of active ingredient: telmisartan		**Page:**	**Number:**	
Ref. to Documentation:	**Volume:**	**Page:** xxx **to** xxxx		**Addendum No.:**
Report date: 13 September 1999	**Number:** U99-3162	**Study period (years):** 16 April 1998 to 12 December 1998		

Title of Study: A Prospective Randomized Open-Label Blinded End point (PROBE) Trial Comparing MICARDIS® (telmisartan) (80 mg QD) and Valsartan (80 mg QD) in Patients with Mild-to-Moderate Hypertension Using Ambulatory Blood Pressure Monitoring.

Investigator: Multicentre study without official designation of a Principal or Coordinating Investigator, See section 6 and 16.1.4

Study center(s): Multicentre study without official designation of a Principal or Coordinating Investigator, See section 6 and 16.1.4

Publication (reference): N/A

Clinical phase: IIIb

Objectives: The primary aim of the trial was to demonstrate that telmisartan is superior to valsartan in lowering ambulatory diastolic and/or systolic blood pressures in the last six hours of the dosing interval. Secondary objectives included evaluations of: 1) the changes from baseline in diastolic and systolic blood pressures during other times during the 24-hour ABPM profile; 2) the changes from baseline in seated trough diastolic and systolic blood pressures as measured by manual cuff sphygmomanometer; 3) responder rates.

Methodology: Prospective, randomized, open-label, blinded end point (PROBE), fixed dose, parallel group comparison trial, using ABPM.

No. of subjects entered:	450 planned, 225 in each treatment group
total:	426 randomized
each treatment:	214 telmisartan; 212 valsartan

Diagnosis and main criteria for inclusion: Mild-to-moderate hypertension defined as the following: a mean seated DBP ≥95 mmHg and ≤114 mmHg, a mean seated SBP ≥140 mmHg and ≤200 mmHg, and 24-hour mean ABPM blood pressure ≥130/85 mmHg at the end of a four-week placebo run-in period.

Test product:	MICARDIS® (telmisartan)
Dose:	80 mg once daily
mode of admin.:	oral
batch no.:	Lot No. PD-1840
Duration of treatment:	8 weeks
Reference therapy:	Diovan® (valsartan)
dose:	80 mg once daily
mode of admin.:	oral
batch no.:	Lot No. 166016

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Criteria for evaluation:

Efficacy:

Primary: Changes from baseline in diastolic and systolic blood pressures during the last six hours of the 24-hour dosing interval, as measured by ambulatory blood pressure monitoring (ABPM).

Secondary: Changes from baseline in diastolic and systolic blood pressures during other times during the 24-hour ABPM profile, changes from baseline in seated trough diastolic and systolic blood pressures as measured by manual cuff sphygmomanometer, and responder rates.

Safety: Physical examination, laboratory parameters, 12-lead ECG, blood pressure and heart rate monitoring and evaluation of adverse events.

Statistical methods: Analysis of covariance; Mantel-Haenszel test; tabulation of adverse events and changes from baseline in ECG, physical exam, and laboratory parameters, summarized by treatment group.

SUMMARY – CONCLUSIONS:

Efficacy results: The results of this trial indicate that telmisartan 80 mg is superior to valsartan 80 mg in lowering diastolic blood pressure during the last six hours of the 24-hour dosing interval. The adjusted mean decrease in diastolic blood pressure over the last six hours, relative to baseline, was 7.5 mmHg for patients treated with telmisartan 80 mg. For patients treated with valsartan 80 mg, the adjusted mean decrease in diastolic blood pressure was smaller, 5.2 mmHg. The difference between the telmisartan and valsartan patients was 2.3 mmHg with this difference being statistically significant ($p<0.01$). There was not a statistically significant difference (defined as $p\leq0.05$) between treatment groups in the extent to which treatment lowered systolic blood pressure during the last six hours of the dosing interval ($p=0.14$).

A number of secondary analyses demonstrated statistically significant differences between the two treatment groups, indicating greater efficacy of telmisartan 80 mg. For example, for the 24-hour mean ABPM data, telmisartan was statistically significantly better than valsartan in lowering both diastolic and systolic blood pressures. In fact, the diastolic and systolic blood pressure reductions produced by telmisartan 80 mg were greater than those produced by valsartan 80 mg throughout most of the 24-hour period. The diastolic and systolic blood pressure reductions produced by telmisartan 80 mg were statistically significantly better than those produced by valsartan 80 mg for "Morning" (06:00–11:59) and "Daytime" (06:00–21:59) ABPM measures ($p <0.01$). However, during the "Nighttime" period (22:00–05:59) when blood pressures tend to decrease ("dip") in most people, the difference between telmisartan and valsartan was not so large. The slightly greater blood pressure reductions produced by telmisartan compared to valsartan during this period reached statistical significance in only one comparison; for diastolic blood pressure in the intent-to-treat analysis.

The decreases in manually measured trough cuff blood pressures produced by telmisartan 80 mg were greater than those produced by valsartan 80 mg, and these differences were statistically significant for both diastolic and systolic blood pressures. Systolic blood pressures were reduced, relative to baseline, by an average of 13.5 mmHg for patients in the telmisartan group, but only by 9.7 mmHg for patients in the valsartan group. Similarly, diastolic blood pressures were reduced by 8.9 mmHg for telmisartan patients, but only by 7.1 mmHg for valsartan patients.

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SUMMARY – CONCLUSIONS: (Continued)

Efficacy results: (Continued)
A positive "DBP response" (defined as trough-cuff DBP mean <90mmHg or a reduction from baseline of at least 10 mmHg) was achieved by 58.5 % of telmisartan patients but only 44.3% of valsartan patients, and this difference was statistically significant. Likewise, a significantly higher percentage of telmisartan patients (47.2%) attained "DBP control" (defined as trough-cuff DBP mean <90mmHg) compared to valsartan patients (32.1%).

There were no statistically significant differences between the two treatment groups in treatment-induced changes in pulse rate, which tended to be small (less than 1 bpm).

Safety results: Both treatments were well tolerated, with safety profiles similar to patients treated with placebo in previous studies. (U97-3132; U98-3144) The only exception to this was with respect to headache, which had a lower rate of occurrence in this study (10.3%) than reported for placebo patients in other hypertension studies (17.4 %). The most frequently reported adverse events were headache and upper respiratory tract infection (6.6%). A very small percentage of patients (2.8%) withdrew from the study due to an adverse event.

Conclusions: Both treatments were effective and well tolerated in this patient population. Telmisartan 80 mg was superior to valsartan 80 mg in reducing diastolic blood pressure during the last six hours of the 24-hour dosing interval. Secondary analyses indicated that telmisartan 80 mg was generally superior to valsartan 80 mg in reducing both diastolic and systolic blood pressures over most of the 24-hour dosing interval. An exception to this was during the nocturnal "dip" in blood pressures, during which time both treatments were roughly equally effective. Telmisartan 80 mg lowered blood pressure over the entire 24-hour dosing interval, including during the early morning period when blood pressures tend to rise.