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 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 July 2001	**Number:** U01-3170	**Study period (years):** 29 March 2000 to 15 December 2000		

Title of study:	A Prospective, Randomized, Double-Blind, Double-Dummy, Titration-to-Response Trial Comparing MICARDIS® (telmisartan) (40 & 80 mg QD) and COZAAR® (losartan) (50 & 100 mg QD) in Patients with Mild-to-Moderate Hypertension using Ambulatory Blood Pressure Monitoring.
Investigator:	Multicenter study without official designation of a Principal or Coordinating Investigator, see section 6 and 16.1.4
Study center(s):	Multicenter study without official designation of a Principal or Coordinating Investigator, see section 6 and 16.1.4.
Publication (reference):	N/A
Clinical phase:	IV
Objectives:	The primary aim of the trial was to determine if MICARDIS® (telmisartan 40-80 mg) is superior to COZAAR® (losartan 50 – 100 mg) in lowering ambulatory diastolic blood pressure (DBP) during the last 6 hours of the 24-hour dosing interval as measured by ABPM after 8-weeks treatment. Secondary objectives included evaluations of: 1) change from baseline in mean systolic blood pressure (SBP) during the last 6 hours of the 24-hour dosing interval as measured by ABPM, 2) changes from baseline in DBP and SBP during other periods during the 24-hour dosing interval, 3) changes from baseline in mean, seated, trough DBP and SBP as measured by manual cuff sphygmomanometer, 4) responder rates based on both ABPM and in-clinic trough cuff blood pressure.
Methodology:	Prospective, randomized, double-blind, double-dummy, titration-to-response, parallel group, comparison trial, using ABPM.
No. of subjects entered:	340 planned, 170 in each treatment group
total:	333 randomized
each treatment:	172 telmisartan; 161 losartan
Diagnosis and main criteria for inclusion:	Patients age 18 years and older with mild-to-moderate hypertension defined as: a mean seated DBP ≥95 mmHg and ≤109 mmHg, and 24-hour ABPM mean DBP ≥85 mmHg.
Test product:	telmisartan
dose:	40–80 mg, once daily
mode of admin.:	Tablets p.o.
batch no.:	Lot No. PD-1954 (T40); PD-1955 (T80)
Duration of treatment:	8 weeks

Name of company: Boehringer Ingelheim		**Tabulated Study Report**		**(For National Authority Use only)**
Name of finished product: MICARDIS®		**SUPPLEMENTARY SHEET**		
Name of active ingredient: telmisartan		**Page:**	**Number:**	
Ref. to Documentation:	**Volume:**	**Page:** xxx **to** xxxx		**Addendum No.:**
Report date: 13 July 2001	**Number:** U01-3170	**Study period (years):** 29 March 2000 to 15 December 2000		

Reference therapy:	Cozaar® (losartan)
dose:	50–100 mg, once daily
mode of admin.:	Tablets p.o.
batch no.:	Lot No. PD-1958
Criteria for evaluation:	
Efficacy:	**Primary:** Change from baseline in diastolic blood pressure (DBP) during the last 6 hours of the 24-hour dosing interval, as measured by ambulatory blood pressure monitoring (ABPM). **Secondary:** Change from baseline in systolic blood pressure (SBP) during the last 6 hours of the 24-hour dosing interval, as measured by ABPM; Changes from baseline in DBP and SBP during other periods during the 24-hour dosing interval; Changes from baseline in mean seated trough DBP and SBP as measured by manual cuff sphygmomanometer; Responder rates based on both ABPM and in-clinic trough cuff blood pressure.
Safety:	Evaluation of adverse events, blood pressure, and heart rate monitoring
Statistical methods:	Analysis of covariance; Mantel-Haenszel test; tabulation of adverse events summarized by treatment group.

SUMMARY - CONCLUSIONS:

Efficacy results:

The results of this trial indicate that telmisartan is superior to losartan in lowering DBP during the last six hours of the 24-hour dosing interval in patients with mild-to-moderate hypertension treated for eight weeks and for whom dose of study medication was titrated upward from the recommended starting dose if blood pressure was not adequately controlled after the first four weeks of treatment. For this, the primary endpoint of the study, telmisartan was found to have a mean change from baseline of –7.1 mmHg while for losartan the mean change from baseline was –4.9 mmHg, with the difference of 2.2 mmHg being statistically significant (p=0.01). Similar results were obtained for change from baseline in the last 6-hour ABPM mean SBP with a statistically (p=0.03) greater reduction from baseline for telmisartan (-9.9 mmHg) than for losartan (-7.2 mmHg). Both of these statistically significant differences were found even though a greater percentage of losartan patients (68.2%) compared to telmisartan patients (58.4%) required titration and were thus on the higher dose at the final measurements.

Additionally, although statistical significance ($p \leq 0.05$) was only achieved for a few of the secondary endpoints, telmisartan was consistently found to have changes from baseline in blood pressure that were greater than those observed

Name of company: Boehringer Ingelheim		**Tabulated Study Report**		**(For National Authority Use only)**
Name of finished product: MICARDIS®		**SUPPLEMENTARY SHEET**		
Name of active ingredient: telmisartan		**Page:**	**Number:**	
Ref. to Documentation:	**Volume:**	**Page:** xxx **to** xxxx		**Addendum No.:**
Report date: 13 July 2001	**Number:** U01-3170	**Study period (years):** 29 March 2000 to 15 December 2000		

	for losartan, as well as consistently greater response rates. Secondary endpoints that achieved statistical significance were: "morning" (06:00-11:59) ABPM mean DBP (changes from baseline of –7.3 and –5.5 mmHg for telmisartan and losartan, respectively; p=0.03), 4-week, 'low dose' in-clinic trough DBP (changes from baseline of –8.9 and –7.2 mmHg for telmisartan and losartan, respectively; p=0.04), end-of-study in-clinic trough SBP (changes from baseline of –9.0 and –7.4 mmHg for telmisartan and losartan, respectively), and 4-week 'low dose' in-clinic DBP response (i.e. DBP <85 mmHg and/or a reduction from baseline >10mmHg with response rates of 48.3% and 36.5% for telmisartan and losartan, respectively). In general, when evaluating the demographic characteristics of age group (<65 years old and ≥65 years old), gender, and race group (black and non-black), the differences between telmisartan and losartan in the changes from baseline in blood pressure (ABPM and/or in-clinic trough measurements) were similar for the different subgroups. Of special interest, the decreases in blood pressure for both the telmisartan and losartan groups were less for black patients than that for non-black patients but with the mean reductions for losartan black patients of -1.1 mmHg and -1.8 mmHg for DBP and SBP, respectively, not found to be significantly different from zero (p=0.46 and p=0.42, respectively). Overall, these results are in agreement with previous studies which indicate that telmisartan, administered once per day, is effective in reducing blood pressure for the full duration of the 24-hr dosing interval, including during the early morning hours.
Safety results:	Both treatments were well tolerated, with safety profiles similar to those of patients treated with placebo in previous studies. The only exception to this was with respect to headache, which had a lower rate of occurrence in this study than reported for placebo patients in other hypertension studies. In this study, only 2.3% of telmisartan-treated patients and 8.1% of losartan-treated patients experienced one or more headaches while on active treatment, compared to 17.4% of placebo patients in previous studies. The most frequently reported adverse events were headache,dizziness, and coughing. A very small percentage (2.1%) of patients withdrew from the study due to an adverse event.
Conclusions:	In conclusion, telmisartan is superior to losartan in reducing diastolic blood pressure during the last six hours of the 24-hour dosing interval in patients treated for eight weeks who were allowed to titrate to the respective higher dose if necessary after four weeks on the starting dose. As well, the preponderance of the results suggest that telmisartan may be superior to losartan in reducing both diastolic and systolic blood pressure throughout the entire 24-hour dosing interval. Further, once daily dosing of either telmisartan or losartan was found to be well tolerated in this patient population.