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 Pharma KG		**Tabulated Study Report**		**(For National Authority Use only)**
Name of finished product: Micardis®				
Name of active ingredient: Telmisartan		**Page:** 1	**Number:**	
Ref. to Documentation:	**Volume:**	**Page:** to		**Addendum No.:**
Report date: 30 September 1999	**Number:**	**Study period (years):** 07 Apr 1998 – 29 Dec 1998		

Title of study:	A Prospective Randomised Open-Label Blinded Endpoint Trial Comparing Telmisartan (Micardis®) 80 mg and Losartan 50 mg + Hydrochlorothiazide 12.5 mg (Lorzaar plus®, Hyzaar®) in Patients with Mild-to-Moderate Essential Hypertension Using Ambulatory Blood Pressure Monitoring (OTELLOH-Study)
Investigator:	[redacted]
Study centre(s):	67
Publication (reference):	
Clinical phase:	IIIb
Objectives:	Primary objective: to demonstrate that telmisartan 80 mg is not inferior compared to losartan 50 mg + HCTZ 12.5 mg in lowering 24-hour mean diastolic blood pressure as measured by ABPM (ambulatory blood pressure monitoring) in patients with mild to moderate primary hypertension (i.e. telmisartan 80 mg reduces the 24 hour ABPM mean DBP by at most 3.0 mmHg less than that associated with losartan 50 mg + HCTZ 12.5 mg). Secondary objective: to demonstrate that telmisartan is not inferior compared to losartan + HCTZ on the following variables: decrease in 24-hour mean systolic blood pressure as measured by ABPM in patients with mild to moderate essential hypertension; changes from baseline in systolic and diastolic blood pressures during other time periods during the 24-hour ABPM profile, changes from baseline in trough systolic and diastolic blood pressures measured by cuff sphygmomanometer at the end of treatment; measures of safety such as changes in pulse rate, incidence of adverse events, results of physical examinations, ECGs, and laboratory tests.
Methodology:	Prospective randomised open-label blinded endpoint (PROBE) design, parallel group comparison trial, using once daily dosing.
No. of subjects entered:	
total:	715 randomised patients
each treatment:	351 Telmisartan 80 mg, 363 Losartan 50 mg + HCTZ 12.5 mg
Diagnosis and main criteria for inclusion:	Mild to moderate hypertension defined as a mean seated DBP ≥ 95 mmHg and ≤ 114 mmHg measured by cuff sphygmomanometer and a 24-hour mean DBP ≥ 85 mmHg measured by ABPM at the end of a four-week placebo period.

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Name of active ingredient: Telmisartan		**Page:** 3	**Number:**	
Ref. to Documentation:	**Volume:**	**Page:** to		**Addendum No.:**
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Test product:	Telmisartan
dose:	80 mg
mode of admin.:	PO
batch no.:	9970058
Duration of treatment:	6 weeks
Reference therapy:	Losartan + HCTZ
dose:	50 mg Losartan + 12.5 mg HCTZ
mode of admin.:	PO
batch no.:	974673
Criteria for evaluation:	
Efficacy:	Changes from baseline in mean 24-hour systolic (SBP) and diastolic blood pressure (DBP) measured by ABPM at the end of treatment, changes from baseline in SBP and DBP during other time periods of the 24-hour ABPM profile and changes from baseline in trough systolic and diastolic blood pressures at the end of the treatment period, as measured by cuff sphygmomanometer.
Safety:	Evaluation of adverse events, pulse rate, physical examination, laboratory parameters, 12-lead ECG.
Statistical methods:	The null hypothesis of therapeutical inferiority of telmisartan 80 mg vs. the combination of losartan 50 mg + HCTZ 12.5 mg was to be rejected if the one-sided 95 %-confidence interval (open to the right) for the difference between changes in 24-hour ABPM means of diastolic BP excluded a treatment difference of 3.0 mmHg or more. The mean squared error (MSE) from an ANCOVA model with baseline as covariate and country and treatment as main effects was taken as measure of variability for calculating the confidence interval.

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SUMMARY - CONCLUSIONS:

Efficacy results:

In the evaluable ABPM population, which is the primary analysis population in this therapeutic non-inferiority trial, the 24-hour mean ABPM DBP was reduced from 93.4 (SD 6.7) mmHg at baseline by 8.2 (SD 6.4) mmHg to 85.2 (SD 7.8) mmHg in the group treated with telmisartan 80 mg, whereas in the group treated with losartan 50 mg + HCTZ 12.5 mg the 24-hour mean DBP was reduced from 94.0 (SD 6.5) mmHg by 10.4 (SD 6.3) mmHg to 83.6 (SD 8.2) mmHg. The mean difference in DBP change between both treatment groups was -2.1, adjusted for baseline values and country, with a one-sided 95 % confidence interval of (-3.0, ∞), i.e. the confidence interval excludes a treatment difference of 3.0 mmHg or more. The intent-to-treat analysis revealed consistent results with a tighter confidence interval of (-2.7, ∞). The analyses of key secondary endpoints (morning ABPM mean DBP, trough cuff DBP, DBP goal response < 90 mmHg) confirmed the primary objective of non-inferiority.

Safety results:

The overall incidence rate of AEs was equal for both treatment groups (telmisartan, 88 out of 351 patients, 25.1 %; losartan + HCTZ, 91 out of 363 patients, 25.1 %).

Conclusions:

The study achieved the primary objective to demonstrate non-inferiority of treatment with telmisartan 80 mg compared to the fixed dose combination losartan 50 mg + HCTZ 12.5 mg according to the definitions of the study protocol.

The results were confirmed by analysis of secondary endpoints of efficacy.

The favourable safety profile of both treatments was confirmed.