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: MICARDIS®			
Name of active ingredient: BIBR 277 SE, telmisartan		**Page:** 1 of 3	**Synopsis No.:**
Module:		**Volume:**	
Report date: 21 APR 2009	**Trial No. / U No.:** 502.557/U09-3222-01	**Date of trial:** 29 SEP 2008- 09 DEC 2008	**Date of revision :** Not applicable

Title of trial:	Bioequivalence of the telmisartan 80 mg film-coated tablet compared with two tablets of the telmisartan 40 mg conventional tablet following oral administration in healthy male volunteers (an open-label, randomised, single-dose, two-sequence, four-period replicated crossover study)
Principal/Coordinating Investigator:	[redacted]
Trial sites:	[redacted] [redacted] Japan
Publication (reference):	Data of this study has not been published
Clinical phase:	I
Objectives:	To demonstrate the bioequivalence of the telmisartan 80 mg film-coated tablet vs. two tablets of the telmisartan 40 mg conventional tablet
Methodology:	Open-label, randomized, single-dose, two-sequence, four-period replicated crossover design
No. of subjects:	
planned:	Entered: 64
actual:	Enrolled: 72 Treatment sequence 1 (Telmisartan 80mg film-coated tablet): entered: 32 treated: 32 analysed (for primary endpoint):32 Treatment sequence 2 (Two tablets of telmisartan 40mg conventional tablet): entered: 32 treated:32 analysed (for primary endpoint):32
Diagnosis and main criteria for inclusion:	Healthy male volunteers, age ≥20 and ≤35 years, BMI range ≥18.0 and ≤25.0 kg/m^2
Test product:	Telmisartan 80 mg film-coated tablet
dose:	80 mg
mode of admin.:	Oral administration with 150 mL water after overnight fast
batch no.:	08020

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Reference therapy:	Two tablets of telmisartan 40 mg conventional tablet
dose:	80 mg
mode of admin.:	Oral administration with 150 mL water after overnight fast
batch no.:	08025
Duration of treatment:	One day (single dose administration) for each treatment
Criteria for evaluation:	
Efficacy / clinical pharmacology:	Pharmacokinetics Primary endpoints: AUC_{0-tz} and C_{max} Secondary endpoints: $AUC_{0-\infty}$, t_{max}, λ_z, $t_{1/2}$ and MRT_{po}
Safety:	Physical examination, vital signs (blood pressure, pulse rate, body temperature), ECG, laboratory tests and adverse events
Statistical methods:	Two-sided 90% confidence intervals for the intra-subject ratio (as estimated by the geometric mean [gMean] of the ratio) of each of AUC_{0-tz} and C_{max} were calculated to determine whether the confidence intervals were contained in the acceptance range of 80% to 125% for bioequivalence. Additionally, the corresponding point estimators (gMeans) for the median intra-subject ratios were provided. The statistical analysis based on a four-period replicated crossover design was an analysis using a mixed effect model on log transformed parameters including "sequence", "period", and "treatment" as fixed effect and "subject within sequence" as random effect, where the difference in mean between the test product and the reference product were estimated by using the restricted maximum likelihood (REML) method. In general, for continuous parameters, descriptive statistics were calculated by treatment, treatment and period, or sequence, for categorical (or categorised) parameters, frequencies were tabulated by treatment, treatment and period, or sequence.

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SUMMARY – CONCLUSIONS:

Efficacy / clinical pharmacology results: The adjusted gMean ratio (90% confidence interval) of telmisartan 80 mg film-coated tablet to two tablets of telmisartan 40 mg conventional tablet was 103.0% (95.5-111.1%) for C_{max} and 101.3% (98.6-104.1%) for AUC_{0-tz}.

Safety results: No deaths or serious adverse events occurred in this trial.

In this trial, nine subjects experienced 14 adverse events but all were mild in intensity. Three subjects experienced four adverse events (two events were dizziness and two events were hypotension), which were considered related to the investigational product by the investigator. But the events disappeared in a short time without treatment.

In individual subjects, there were some values for SBP and DBP that decreased more than 20mmHg from the baseline. This observation was most pronounced in the eight hour point after investigational product administration. Towards the 72 hour point, most subjects had returned to baseline without any symptoms.

No findings resulting in adverse events were detected in ECGs.

Conclusions: The 90% confidence intervals of the ratio for C_{max} and AUC_{0-tz} were within the acceptance range for bioequivalence (80-125%). Therefore, bioequivalence was proven between the telmisartan 80 mg film-coated tablet and the two tablets of telmisartan 40 mg conventional tablet in this trial.

In individual subjects in both treatment sequences, there were some values for SBP and DBP that decreased more than 20 mmHg from the baseline. This observation was most pronounced in the eight hour point after investigational product administration. Towards the 72 hour point, most subjects had returned to baseline without any symptoms.

Telmisartan 80 mg film-coated tablet therapy and two tablets of telmisartan 40 mg conventional tablet therapy were both well tolerated by healthy Japanese male subjects.