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**		
Name of finished product: Micardis®				
Name of active ingredient: BIBR 277 SE, Telmisartan		**Page:**	**Number:**	
Ref. to Documentation:	**Volume:**	**Page:**		**Addendum No.:**
Report date: 24 August 2007	**Number:** U07-3292	**Study period (dates):** 01 January 2007 - 30 April 2007		

Title of study:	Bioequivalence of the 40 mg telmisartan film-coated tablet compared with the conventional 40 mg telmisartan tablet following oral administration in healthy male volunteers (an open-label, randomised, single-dose, two-sequence, four-period replicated crossover study)
Investigator:	[redacted]
Study centre:	[redacted]
Publication (reference):	Data of this study have not been published
Clinical phase:	I
Objectives:	To demonstrate the bioequivalence of the 40 mg telmisartan film-coated tablet vs. the conventional 40 mg telmisartan tablet
Methodology:	Open-label, randomised, single-dose, two-sequence, four-period replicated crossover design
No. of subjects:	
planned:	30
actual:	30 Treatment sequence 1: telmisartan 40 mg film-coated tablet → conventional telmisartan 40 mg tablet → conventional telmisartan 40 mg tablet → telmisartan 40 mg film-coated tablet enrolled : 15 entered : 15 treated : 15 Treatment sequence 2: conventional telmisartan 40 mg tablet → telmisartan 40 mg film-coated tablet → telmisartan 40 mg film-coated tablet → conventional telmisartan 40 mg tablet enrolled : 15 entered : 15 treated : 15

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Diagnosis and main criteria for inclusion:	Healthy males were selected according to the following criteria: 1. Complete medical history, including physical examination, vital signs (blood pressure, pulse rate, body temperature), 12-lead ECG and clinical laboratory tests 1.1 No findings deviating from normal, or of clinical relevance 1.2 No evidence of a clinically relevant concomitant disease 2. Age ≥ 20 and ≤ 35 years 3. BMI (body mass index) ≥ 17.6 and ≤ 26.4 kg/m² 4. Signed and dated written informed consent prior to admission to the study in accordance with GCP and the local legislation <Rationale for setting the inclusion criteria> Criterion 1 was for defining a healthy volunteer; criteria 2 and 3 were to balance demographics to investigate pharmacokinetics of telmisartan and criterion 4 was for targeting a healthy volunteer because there were no benefits of the study for the subjects.
Test product: **dose:** **mode of admin.:** **batch no.:**	Telmisartan 40 mg film-coated tablet 40 mg Oral administration after an overnight fast with 150 mL water 06079
Duration of treatment:	One day (single dose po) for each treatment by 2-week washout period between treatments
Reference product: **dose:** **mode of admin.:** **batch no.:**	Telmisartan 40 mg conventional tablet 40 mg Oral administration after an overnight fast with 150 mL water 06080
Criteria for evaluation: **Pharmacokinetics:**	 Pharmacokinetics Primary endpoints: AUC_{0-tz} and C_{max} Secondary endpoints: $AUC_{0-\infty}$, t_{max}, λ_z, $t_{1/2}$ and MRT_{po}

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Safety:	Physical examination, vital signs (blood pressure, pulse rate, body temperature), 12-lead ECG, clinical laboratory tests and adverse events
Statistical methods:	Two-sided 90% confidence intervals for the intra-subject ratio (as estimated by the geometric mean of the ratio) of each of AUC_{0-tz} and C_{max} were calculated to determine whether the confidence intervals are contained in the acceptance range of 80-125% for bioequivalence. Additionally, the corresponding point estimators (geometric means) 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 differences in test and reference means were estimated using the restricted maximum likelihood method. For all numerical parameters, descriptive statistics were calculated and for all categorical parameters, frequencies were tabulated.

SUMMARY – CONCLUSIONS:

Pharmacokinetics results:	The geometric mean values of C_{max} and AUC_s for the film-coated tablet were lower than those for the conventional tablet. The adjusted geometric mean ratio (90% confidence interval) of film-coated tablet to conventional tablet was 77.5% (68.5-87.6%) for C_{max} and 90.6% (84.4-97.2%) for AUC_{0-tz}. The 90% confidence interval of the ratio for AUC_{0-tz} was within the acceptance range for bioequivalence (80-125%), whereas that for C_{max} was not within the acceptance range.
Safety results:	Five subjects experienced eight adverse events in total. There was no serious adverse event. There was only one adverse event related to the study drug: Blood pressure decreased. It caused by enhancement of the blood pressure-lowering effect of the drug under physical deconditioning of the subject due to the nasopharyngitis. No clinically significant changes were found in laboratory parameters, vital signs, or ECG. Amylase increased in one subject. The abnormal value was considered unrelated to the test drug because the subject presented no clinical findings and baseline value was near the upper limit of normal. It was concluded that there were no clinically significant findings. Both the film-coated tablet and the conventional tablet were well tolerated by healthy subjects.

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Conclusions:	The 90% confidence interval of the ratio for AUC_{0-tz} was within the acceptance range for bioequivalence (80-125%), whereas that for C_{max} was not within the acceptance range. Therefore, bioequivalence between the film-coated tablet and the conventional tablet was not proven in this trial. There were no clinically significant findings regarding safety. Both the film-coated tablet and the conventional tablet were well tolerated by healthy subjects.