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:			
Name of active ingredient: Telmisartan + hydrochlorothiazide		**Page:** 1 of 3	**Synopsis No.:**
Module:		**Volume:**	
Report date: 12 DEC 2008	**Trial No. / U No.:** 502.571/ U08-3801-01	**Date of trial:** 22 JUL 2008 – 15 OCT 2008	**Date of revision** (if applicable)**:**

Title of trial:	Bioequivalence of telmisartan administrated in two different ways: either in telmisartan 80 mg/HCTZ 12.5 mg fixed-dose combination tablet or as two telmisartan 40 mg tablets (an open-label, randomised, single-dose, four-period replicated crossover study)
Principal/Coordinating Investigator:	[redacted]
Trial sites:	[redacted] Japan
Publication (reference):	The data of this trial have not been published.
Clinical phase:	I
Objectives:	To establish bioequivalence of telmisartan orally administrated in two different ways: either with a telmisartan 80 mg/hydrochlorothiazide (HCTZ) 12.5 mg fixed-dose combination tablet or with two telmisartan 40 mg tablets
Methodology:	Open-label, randomised, single-dose, four-period replicated crossover design
No. of subjects:	
planned:	To be entered: 64 subjects
actual:	Enrolled, 117 subjects; entered, 64 subjects Treatment sequence 1: entered, 32; treated, 32; analysed (for primary endpoint), 32 Treatment sequence 2: entered, 32; treated, 32; analysed (for primary endpoint), 32
Diagnosis and main criteria for inclusion:	Healthy male volunteers, age ≥20 and ≤35 years, body mass index (BMI) ≥18.0 and ≤25.0 kg/m^2, body weight ≥50 kg
Test product:	A tablet of telmisartan 80 mg/HCTZ 12.5 mg fixed-dose combination
dose:	Telmisartan 80 mg and HCTZ 12.5 mg
mode of admin.:	Oral

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batch no.:	08047
Reference therapy:	Two tablets of telmisartan 40 mg
dose:	Telmisartan 80 mg
mode of admin.:	Oral
batch no.:	08046
Duration of treatment:	Single dose administration each in 4 treatment periods
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, and body temperature), 12-lead electrocardiogram (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 [gMean] of the ratio) of each of AUC_{0-tz} and C_{max} was 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 differences 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:

Clinical pharmacology results: The adjusted gMean ratio (90% confidence interval) of telmisartan 80 mg/HCTZ 12.5 mg fixed-dose combination therapy to telmisartan 80 mg monotherapy was 93.9% (86.6% to 101.9%) for C_{max} and 104.3% (101.3% to 107.4%) for AUC_{0-tz}. The 90% confidence intervals for C_{max} and AUC_{0-tz} were within the acceptance range for bioequivalence (80% to 125%).

Safety results: In this trial, 3 adverse events occurred: abnormal feeling, nasopharyngitis, and upper respiratory tract infection, all of which were mild in intensity. Only abnormal feeling was considered related to the investigational product by the investigator.

Neither deaths nor serious adverse events occurred in this trial.

Two subjects experienced adverse events leading to the discontinuation of the investigational product, whose relationship with the investigational product was denied by the investigator.

No clinically significant changes from the baseline were detected either in clinical laboratory test parameters or in vital signs.

Conclusions: The 90% confidence intervals of the ratio for C_{max} and AUC_{0-tz} were within the acceptance range for bioequivalence (80% to 125%). Therefore, bioequivalence of telmisartan was established between telmisartan 80 mg/HCTZ 12.5 mg fixed-dose combination therapy and telmisartan 80 mg monotherapy in this trial.

Telmisartan 80 mg/HCTZ 12.5 mg fixed-dose combination therapy and telmisartan 80 mg monotherapy were both well tolerated by healthy Japanese male subjects.