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 4	**Synopsis No.:**
Module:		**Volume:**	
Report date: 8 DEC 2008	**Trial No. / U No.:** 502.569 / U08-3792-01	**Date of trial:** 19 July 2008 – 25 August 2008	**Date of revision** (if applicable)**:**

Title of trial:	Influence of food on the bioavailability of telmisartan 40 mg/HCTZ 12.5 mg fixed-dose combination and of telmisartan 80 mg/HCTZ 12.5 mg fixed-dose combination in Japanese healthy male volunteers (an open-label, randomised, single-dose, two-way crossover study)
Principal/Coordinating Investigator:	[redacted]
Trial sites:	[redacted] Japan
Publication (reference):	Data of this trial have not been published.
Clinical phase:	I
Objectives:	To investigate the relative bioavailability and pharmacokinetics of the fixed-dose combination tablets (telmisartan 40 mg/HCTZ 12.5 mg and telmisartan 80 mg/HCTZ 12.5 mg) after food intake in comparison with those in the fasting state in healthy Japanese male volunteers
Methodology:	Open-label, randomised, single-dose, two-way crossover design
No. of subjects:	
planned:	to be enrolled: 32 subjects; to be entered: 32 subjects
actual:	enrolled: 71 subjects; entered: 32 subjects Treatment with telmisartan 40 mg/HCTZ 12.5 mg: entered: 16 subjects; treated: 16 subjects; analysed (for primary endpoint): 16 subjects; Treatment with telmisartan 80 mg/HCTZ 12.5 mg: entered: 16 subjects; treated: 16 subjects; analysed (for primary endpoint): 16 subjects
Diagnosis and main criteria for inclusion:	Healthy male volunteers; age, ≥20 and ≤35 years; body weight, ≥50 kg; Body mass index (BMI) range, ≥18.0 and ≤25.0 kg/m^2
Test therapy:	Telmisartan 40 mg/HCTZ 12.5 mg fixed-dose combination, fed, telmisartan 80 mg/HCTZ 12.5 mg fixed-dose combination, fed

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dose:	Telmisartan 40 mg and HCTZ 12.5 mg, telmisartan 80 mg and HCTZ 12.5 mg
mode of admin.:	Oral administration with 150 mL water after a Japanese breakfast
batch no.:	08044 for telmisartan 40 mg/HCTZ 12.5 mg, 08045 for telmisartan 80 mg/HCTZ 12.5 mg
Reference therapy:	Telmisartan 40 mg/HCTZ 12.5 mg fixed-dose combination, fasted, telmisartan 80 mg/HCTZ 12.5 mg fixed-dose combination, fasted
dose:	Telmisartan 40 mg and HCTZ 12.5 mg, telmisartan 80 mg and HCTZ 12.5 mg
mode of admin.:	Oral administration with 150 mL water after an overnight fast for at least 10 hours
batch no.:	08044 for telmisartan 40 mg/HCTZ 12.5 mg, 08045 for telmisartan 80 mg/HCTZ 12.5 mg
Duration of treatment:	One day (single dose po) for each treatment period
Criteria for evaluation:	
Efficacy / clinical pharmacology:	Pharmacokinetic parameters: 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 temprature), 12-lead electrocardiography (ECG), clinical laboratory tests, and adverse events
Statistical methods:	Point estimators (geometric means) of the median intra-subject ratios of AUC_{0-tz} and C_{max} and their two-sided 90% confidence intervals were calculated separately for telmisartan and HCTZ. The statistical model was an analysis of variance model on log transformed parameters including effects for "sequence," "subjects nested within sequences," "period," and "treatment." Confidence intervals were based on the residual error from analysis of variance. In general, descriptive statistics were calculated by treatment, treatment and period, or sequence, for continuous parameters; frequencies were tabulated by treatment, treatment and period, or sequence, for categorical (or categorised) parameters.

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SUMMARY – CONCLUSIONS:

Efficacy / clinical pharmacology results:

When the fixed-dose combination tablet of T40/H12.5 mg or T80/H12.5 mg was taken with food, the bioavailability, as calculated from the geometric mean of AUC_{0-tz} of telmisartan, was on average reduced by 28.6% and 33.4%, respectively, compared with that in the fasted condition. The food effect was noted more clearly in the peak concentration, C_{max}, where the geometric mean of C_{max} of telmisartan was reduced by 61.8% after administration of both T40/H12.5 mg and T80/H12.5 mg. The median t_{max} was delayed for telmisartan in the fed condition.

When the fixed-dose combination tablet of T40/H12.5 mg or T80/H12.5 mg was taken with food, the bioavailability, as calculated from the geometric mean of AUC_{0-tz} of HCTZ, was on average reduced by 13.4% and 12.8%, respectively, compared with that in the fasted condition. Food slightly affected the C_{max}: the geometric mean of C_{max} of HCTZ was reduced by 14.7% after administration of T40/H12.5 mg and 13.4% after administration of T80/H12.5 mg. The median t_{max} of HCTZ was similar in the fasted and the fed conditions.

Safety results:

No deaths, serious adverse events, nor significant adverse events were reported during the trial.

No subjects were withdrawn from the trial.

During the trial, 1 adverse event of hypotension was reported by a subject in the telmisartan 40 mg/HCTZ 12.5 mg dose group while he was treated with the investigational product fasted. The event was mild and transient and disappeared without any treatment. The event was considered drug related by the investigator.

No clinically significant changes from the baseline were noted in blood pressure, pulse rate, body temperature, or laboratory test results.

No findings corresponding to adverse events were noted in ECGs.

Both telmisartan 40 mg/HCTZ 12.5 mg and telmisartan 80 mg/HCTZ 12.5 mg were well tolerated by the healthy Japanese male subjects when they were administered after meal or fasted.

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Conclusions:	The bioavailability of telmisartan was reduced by food intake after single oral administration of telmisartan 40 mg/HCTZ 12.5 mg or telmisartan 80 mg/HCTZ 12.5 mg as fixed-dose combination tablets, compared to that in the fasted condition. The bioavailability of HCTZ was slightly reduced by food intake. These results are similar to previous results with either telmisartan or HCTZ. In conclusion, both telmisartan 40 mg/HCTZ 12.5 mg and telmisartan 80 mg/HCTZ 12.5 mg were safe and well tolerated by the healthy Japanese male subjects when they were administered after meal or fasted.