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: Not applicable		**EudraCT No.:** 2007-002684-26	
Name of active ingredient: BI 10773		**Page:** **1 of 4**	**Synopsis No.:**
Module:		**Volume:**	
Report date: 26 JAN 2009	**Trial No. / U No.:** 1245.3 / U08-1977-01	**Dates of trial:** 17 JAN 2008 – 8 FEB 2008	**Date of revision** (if applicable)**:**

Title of trial:	The effect of food on the bioavailability and pharmacokinetics of BI 10773 tablets, administered as a single dose of 50 mg with and without food to healthy male volunteers in an open-label, randomised intraindividual crossover comparison design
Principal Investigator:	[redacted]
Trial site:	Human Pharmacology Centre, Boehringer Ingelheim Pharma GmbH & Co. KG, Biberach an der Riss, Germany
Publication (reference):	Data of this study have not been published.
Clinical phase:	I
Objectives:	To assess the effect of food on the pharmacokinetics and the extent of absorption of a single dose BI 10773 tablet in healthy subjects
Methodology:	Single dose, open-label, randomised, two-sequence, two-period crossover design
No. of subjects:	
planned:	entered: 14
actual:	entered: 14 Test treatment (T): 50 mg BI 10773 with food: entered: 14 treated: 14 analysed (for primary endpoint): 14 Reference treatment (R): 50 mg BI 10773 fasted: entered: 14 treated: 14 analysed (for primary endpoint): 14
Diagnosis and main criteria for inclusion:	Healthy male subjects, age 18 to 55 years, body mass index 18.5 to 29.9 kg/m^2; Exclusion criteria specific for this study: elevated urinary glucose levels at screening
Test product:	BI 10773 tablet (administered with food)
dose:	50 mg BI 10773 base equivalent (two tablets of 25 mg BI 10773)
mode of admin.:	Oral administration with 240 mL water after a standardised high fat, high calorie breakfast

Name of company: Boehringer Ingelheim		**Tabulated Trial Report**	Boehringer Ingelheim
Name of finished product: Not applicable		**EudraCT No.:** 2007-002684-26	
Name of active ingredient: BI 10773		**Page:** 2 of 4	**Synopsis No.:**
Module:		**Volume:**	
Report date: 26 JAN 2009	**Trial No. / U No.:** 1245.3 / U08-1977-01	**Dates of trial:** 17 JAN 2008 – 8 FEB 2008	**Date of revision** (if applicable)**:**

batch no.:	B063000368, B073000808
Reference therapy:	BI 10773 tablet (administered to fasted subjects)
dose:	50 mg BI 10773 base equivalent (two tablets of 25 mg BI 10773)
mode of admin.:	Oral administration with 240 mL water after an overnight fast of at least 10 hours
batch no.:	B063000368, B073000808
Duration of treatment:	Two days (a single dose for each treatment with a wash-out period of at least seven days between treatments)
Criteria for evaluation:	
Efficacy / clinical pharmacology:	<u>Pharmacokinetic (PK) parameters of BI 10773</u> Primary endpoints: $AUC_{0-\infty}$, C_{max} Secondary endpoints: t_{max}, $t_{½}$, MRT_{po}, CL/F, V_z/F <u>Pharmacodynamic (PD) parameters of BI 10773</u> Glucose in urine, creatinine in urine
Safety:	Physical examination including pre- and post-dose body weight Vital signs (blood pressure, pulse rate) 12-lead electrocardiogram (ECG) Routine laboratory tests including urine glucose and creatinine concentrations, urine osmolality, fluid balance (FB), and glucose bedside test Adverse events (AEs) Assessment of tolerability
Statistical methods:	Descriptive statistics for safety and PK endpoints were calculated. Point estimators (geometric means) of the median intra-subject ratios of $AUC_{0-\infty}$ and C_{max} of BI 10773 and their two-sided 90% confidence intervals were calculated to compare 50 mg BI 10773 under fed with fasted conditions.

Name of company: Boehringer Ingelheim		**Tabulated Trial Report**	Boehringer Ingelheim
Name of finished product: Not applicable		**EudraCT No.:** 2007-002684-26	
Name of active ingredient: BI 10773		**Page:** 3 of 4	**Synopsis No.:**
Module:		**Volume:**	
Report date: 26 JAN 2009	**Trial No. / U No.:** 1245.3 / U08-1977-01	**Dates of trial:** 17 JAN 2008 – 8 FEB 2008	**Date of revision** (if applicable)**:**

SUMMARY – CONCLUSIONS:

Efficacy / clinical pharmacology results: The geometric mean ratios and 90% confidence intervals for $AUC_{0-\infty}$ and C_{max} of BI 10773 under fed and fasted conditions were compared with bioequivalence criteria of 80 to 125%. The extent of absorption met the bioequivalence criteria ($AUC_{0-\infty}$ geometric mean ratio 89.8%, 90% confidence interval 84.5 to 95.5%); however, the rate of absorption was below these bioequivalence criteria (C_{max} geometric mean ratio 70.7%, 90% confidence interval 61.0 to 81.8%). Administration of BI 10773 with food had no relevant effects on the amounts of glucose and creatinine excreted in urine.

Safety results: After administration of single doses of 50 mg BI 10773 to healthy male volunteers under fed and fasted conditions, the number of subjects who experienced AEs was equal in each treatment period (four subjects, 28.6%). The most frequently reported AE was headache; the number of subjects with headache was equal when the drug was given with and without food (two subjects, 14.3%). The investigator considered headache, back pain, and fatigue in two subjects during the fasted treatment period and headache, diarrhoea, nausea, and vomiting in three subjects in the fed treatment period to be possibly related to the treatment medication. One subject experienced moderate nausea and diarrhoea; all other AEs were mild in intensity. One subject continued to experience nasopharyngitis, cough, and toothache at the end of the trial, but follow up was considered sufficient. All other subjects recovered from their AEs. No serious AEs or deaths occurred. Global tolerability was good when BI 10773 was administered with or without food. There were no findings of clinical significance in the clinical laboratory evaluation, vital signs, urine parameters, or 12-lead ECG.

Name of company: Boehringer Ingelheim		**Tabulated Trial Report**	Boehringer Ingelheim
Name of finished product: Not applicable		**EudraCT No.:** 2007-002684-26	
Name of active ingredient: BI 10773		**Page:** 4 of 4	**Synopsis No.:**
Module:		**Volume:**	
Report date: 26 JAN 2009	**Trial No. / U No.:** 1245.3 / U08-1977-01	**Dates of trial:** 17 JAN 2008 – 8 FEB 2008	**Date of revision** (if applicable)**:**

Conclusions:

The objective of this study was to determine the effect of food on the pharmacokinetics of BI 10773 in healthy volunteers. After oral administration of single doses of 50 mg BI 10773 after a high fat, high calorie meal, the extent of absorption was within bioequivalence criteria; however, the rate of absorption was below bioequivalence criteria. Urinary glucose excretion was similar when BI 10773 was administered under fed and fasted conditions.

The safety of single oral doses of 50 mg BI 10773 was good and not affected by administration of the drug with food.

Considering the lack of effect on urinary glucose excretion, the good safety profile, and the fact that the extent of absorption met the bioequivalence criteria, the observed effect of food on pharmacokinetic parameters of BI 10773 was considered not clinically relevant. BI 10773 tablets can therefore be administered with or without food.