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***.

2. SYNOPSIS

Name of company: Boehringer Ingelheim		**Tabulated Study Report**		**(For National Authority Use only)**
Name of finished product: Not applicable				
Name of active ingredient: BIIL 284 BS		**Page:**	**Number:**	
Ref. to Documentation:	**Volume:**	**Page:** to		**Addendum No.:**
Report date: 21 August 2001	**Number:** 543.28	**Study period (years):** October to December 2000		

Title of study:	Randomised 4-way cross-over phase I study to investigate the relative bioavailability of BIIL 284 BS 75 mg boli in comparison to tablet C in fasted condition and after ingestion of a standardised meal in healthy volunteers.
Investigator:	[redacted]
Study centre(s):	Human Pharmacology Centre Ingelheim, Boehringer Ingelheim Pharma KG, Germany
Publication (reference):	Not applicable
Clinical phase:	I
Objectives:	Relative bioavailability, pharmacokinetics, safety and tolerability
Methodology:	4-way cross-over comparison of four treatments, randomised, open-labelled
No. of subjects entered:	
total:	16
each treatment:	BIIL 284 BS 75 mg boli fasted - 16 BIIL 284 BS 75 mg boli fed - 16 BIIL 284 BS 75 mg tablet C fasted - 16 BIIL 284 BS 75 mg tablet C fed – 16
Diagnosis and main criteria for inclusion:	Healthy male volunteers, age 21 – 50 years, Broca-Index: ± 20 %
Test product:	BIIL 284 BS tablets
dose:	75 mg boli
mode of admin.:	Oral in fasted condition and after standard breakfast
batch no.:	B 0F0200A0
Duration of treatment:	One day at each treatment
Reference therapy:	BIIL 284 BS tablets
dose:	75 mg tablet C
mode of admin.:	Oral in fasted condition and after standard breakfast
batch no.:	B 000705

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Criteria for evaluation:

Efficacy: Pharmacokinetic evaluation:

Single-dose pharmacokinetic parameters for BIIL 284 BS metabolite, BIIL 315 ZW, determined by non-compartmental analysis of plasma BIIL 315 ZW concentrations over 72 hours post-dose. Primary parameters, C_{max} and $AUC_{0-\infty}$, and secondary pharmacokinetic parameters, t_{max}, $t_{½}$, MRT_{tot}, CL_{tot}/F and V_z/F of BIIL 315 ZW were determined.

Safety: Blood pressure, pulse rate, ECG, adverse events, laboratory test

Statistical methods: Descriptive analysis, analysis of variance, confidence intervals (CI)

SUMMARY - CONCLUSIONS:

Efficacy results:

Pharmacokinetics:

Both plasma concentrations and primary pharmacokinetic parameters of BIIL 315 ZW were considerably higher following BIIL 284 BS boli formulation administration compared to tablet C. In fasted conditions adjusted mean ratios (boli/tablet C) ranged from 725.8% for C_{max} (CI: 497.7 to 1058.4) to 443.5% for $AUC_{0-\infty}$ (CI: 322.5 to 609.9). In fed conditions adjusted mean ratios (boli/tablet C) ranged from 472.3% for C_{max} (CI: 323.9 to 688.7) to 357.7% for $AUC_{0-\infty}$ (CI: 261.8 to 488.6). Food has a substantial influence on the bioavailability of BIIL 284 BS as either boli or tablet C formulation, with a smaller food effect for the boli formulation ($AUC_{0-\infty}$ ratio (fed/fasted): 160.7%, CI:117.4 to 219.9) compared to tablet C ($AUC_{0-\infty}$ ratio (fed/fasted): 199.2%, CI:145.0 to 273.8). Inter-individual variability in pharmacokinetic parameters and plasma concentrations was moderate to high (C_{max} and $AUC_{0-\infty}$: 41.6 – 118 gCV%) for all treatment groups but was generally higher in the tablet C treatment group. Administration of BIIL 284 BS after food also resulted in decreased inter-individual variability in plasma concentrations.

Safety results:

Due to the observations made in this study BIIL 284 BS was safe and well tolerated in healthy male volunteers following single doses of 75 mg BIIL 284 BS administered as boli formulation in fasted and fed condition and as tablet C in fasted and fed condition. The safety parameters blood pressure, pulse rate, ECG and standard laboratory tests did not reveal any obvious clinically significant drug-related changes. With the conditions investigated in this trial BIIL 284 BS was free of any side effects which would raise objections to further clinical studies in volunteers or patients.

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Conclusions:

BIIL 284 BS was safe and well tolerated in all conditions tested.
The boli formulation appears to be superior to tablet C since it has higher bioavailability in both the fasted and fed states and is slightly less affected by food than tablet C.