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: 10 November 2000	**Number:** 543.3	**Study period (years):** 11/99 to 12/99		

Title of study:	Randomised 3-way cross-over phase I study to investigate the relative bioavailability of BIIL 284 BS 75 mg tablet C and tablet D in comparison to WIF tablet in healthy volunteers.
Investigator:	[redacted]
Study centre(s):	Human Pharmacology Centre Ingelheim, Boehringer Ingelheim Pharma KG, FRG
Publication (reference):	not applicable
Clinical phase:	I
Objectives:	relative bioavailability, pharmacokinetics, safety and tolerability
Methodology:	3-way cross-over comparison of three treatments, randomised, open-labelled
No. of subjects entered:	
total:	12
each treatment:	BIIL 284 BS 75 mg tablet C – 12 BIIL 284 BS 75 mg tablet D – 11 BIIL 284 BS 75 mg WIF tablet – 12
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 (tablet C), 75 mg (tablet D)
mode of admin.:	oral after standard breakfast
batch no.:	B990904 (tablet C), B990909 (tablet D)
Duration of treatment:	one day at each treatment
Reference therapy:	BIIL 284 BS tablets
dose:	75 mg WIF tablet
mode of admin.:	oral after standard breakfast
batch no.:	B990105

Name of company: Boehringer Ingelheim		**Tabulated Study Report**		**(For National Authority Use only)**
Name of finished product: Not applicable		**SUPPLEMENTARY SHEET**		
Name of active ingredient: BIIL 284 BS		**Page:**	**Number:**	
Ref. to Documentation:	**Volume:**	**Page:to**		**Addendum No.:**
Report date: 10 November 2000	**Number:** 543.3	**Study period (years):** 11/99 to 12/99		

Criteria for evaluation:

Efficacy:	not applicable
Safety:	blood pressure, pulse rate, ECG, adverse events, laboratory tests
Pharmacokinetics:	non-compartmental pharmacokinetic analysis. Relative bioavailability of the two test formulations (tablet C and tablet D) as compared to the WIF tablet
Statistical methods:	descriptive analysis

SUMMARY - CONCLUSIONS:

Safety results:

There was no evidence for a treatment dependent increase either in frequency or in intensity of adverse events. Seven of the 12 treated subjects reported 12 adverse events during the study. The most frequent adverse event was fatigue. Safety parameters blood pressure, pulse rate, ECG and standard laboratory tests did not reveal any obvious clinically significant drug-related changes.

Other results:

Pharmacokinetics:

The mean relative bioavailability of tablet C compared to the WIF tablet was 262% (two sided 90% C.I.: 172 - 400%) with regard to C_{max} and 247% (two sided 90% C.I.: 175 - 347%) regarding $AUC_{0-\infty}$ of BIIL 315 ZW. Tablet C showed a slightly higher mean bioavailability of 134% (two sided 90% C.I.: 87 - 207%) with regard to C_{max} and 138% (two sided 90% C.I.: 97 - 196%) regarding $AUC_{0-\infty}$ compared to tablet D.

With regard to t_{max}, elimination half-life and MRT no marked differences in the pharmacokinetic characteristics of BIIL 315 BS were observed between the three administered BIIL 284 BS formulations tablet C, tablet D and WIF tablet.

Interindividual variability in C_{max} (60-84%gCV) and $AUC_{0-\infty}$ (66-86%gCV) of BIIL 315 was consistently high. Highest C_{max} value for BIIL 315 ZW was 116 ng/mL.

Conclusions:

As the results with regard to $AUC_{0-\infty}$ (C_{max}) showed that tablet C provided higher relative bioavailability compared to tablet D and WIF tablet by a factor of 1.38 and 2.47 (1.34 and 2.62) , respectively, it is recommended to use tablet C in further clinical trials. BIIL 284 BS was safe and well tolerated in all treatment groups.