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: ---				
Name of active ingredient: BIIL 284 BS		**Page:**	**Number:**	
Ref. to Documentation:	**Volume:**	**Page:**		**Addendum No.:**
Report date: 6 December 2000	**Number:** 543.5	**Study period (years):** 02/00 – 03/00		

Title of study:	Randomised 3-way cross-over phase I study to investigate the effect of different food compositions (low fat and high fat meal) on bioavailability of BIIL 284 BS 75 mg tablet in healthy male volunteers.	
Investigator:	[redacted]	
Study centre(s):	Human Pharmacology Centre, Boehringer Ingelheim Pharma KG, FRG	
Clinical phase:	I	
Objectives:	Food effect, relative bioavailability, pharmacokinetics, safety and tolerability	
Methodology:	3-way cross-over comparison of three treatments, randomised, open-labelled	
No. of subjects entered:		
total:	24	
each treatment:	BIIL 284 BS 75 mg tablet in fasted condition BIIL 284 BS 75 mg after low fat meal BIIL 284 BS 75 mg after high fat meal	- 23 - 24 - 24
Diagnosis and main criteria for inclusion:	Healthy male volunteers, age 21 - 50 years, Broca-Index: ± 20%	
Test product:	BIIL 284 BS tablet	BIIL 284 BS tablet
dose:	75 mg	75 mg
mode of admin.:	Oral after low fat meal	Oral after high fat meal
batch no.:	B990904	B990904
Duration of treatment:	One day at each treatment	
Reference therapy:	BIIL 284 BS tablet	
dose:	75 mg	
mode of admin.:	Oral in fasted condition	
batch no.:	B990904	

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Criteria for evaluation:

Efficacy:	**Pharmacokinetics:** non-compartmental pharmacokinetic analysis. Relative bioavailability of the tablet after low fat and high fat meal as compared to fasted condition.
Safety:	Blood pressure, pulse rate, ECG, adverse events, laboratory tests
Statistical methods:	Linear model, descriptive analysis

SUMMARY - CONCLUSIONS:

Safety results:

Due to the observations made in this study described in this report BIIL 284 BS was safe and well tolerated in healthy male volunteers following single doses of 75 mg BIIL 284 BS administered as tablet C in fasted condition, after a low fat meal and after a high fat meal. 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.

Other results:

Pharmacokinetics:

A relevant food effect is concluded of BIIL 315 ZW for both fed conditions compared to fasted state for C_{max} (C. I. for ratio low fat/fasted: 278.5 to 526.7, high fat/fasted: 249.5 to 471.9) and $AUC_{0-\infty}$ (C. I. for ratio low fat/fasted: 182.9 to 301.9, high fat/fasted: 183.4 to 302.6). BIIL 315 ZW showed nearly similar C_{max} and AUC0-∞ values following low and high fat meal. Adjusted mean ratios ranged from 89.6% for C_{max} (C. I. for ratio high fat/low fat: 65.5 to 122.6) to 100.2% for $AUC_{0-\infty}$ (C. I.: 78.3 to 128.3). BIIL 315 ZW showed considerable residual variability with regard to C_{max} and $AUC_{0-\infty}$.

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 BIIL 284 BS treatments (fasted/low fat/high fat).

Interindividual variability in C_{max} (80-150% gCV) and $AUC_{0-\infty}$ (74-109%gCV) of BIIL 315 ZW for the two treatments in fed state was consistently high irrespective of food composition. Lowest interindividual variability of C_{max} (80%gCV) and $AUC_{0-\infty}$ (74%gCV) was observed for the low fat treatment.

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Conclusions:

BIIL 284 BS was safe and well tolerated in all conditions.
The results with regard to C_{max} and $AUC_{0-\infty}$ showed a clear food effect. Relative bioavailability after food intake of a low or high fat meal before BIIL 284 BS administration is quite similar but significantly higher compared to fasted conditions (by a factor of about 3). The type of food (low or high fat content) seemed to be of less importance as no clear difference was shown for tablet C for different fed conditions. In order to increase exposure in clinical trials it is therefore recommended to administer BIIL 284 BS together with food.