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 Study Report**		
Name of finished product: -				
Name of active ingredient: BIRB 1017 BS		**Page:**	**Number:**	
Ref. to Documentation:	**Volume:**	**Page:**		**Addendum No.:**
Report date: 26 SEP 2005	**Number:** U05-2132	**Study period (dates):** 31 Aug - 16 Nov 2004		

Title of study:	Safety, tolerability, and pharmacokinetics of single rising oral doses of BIRB 1017 BS (5, 25, 100, 250, 500, and 800 mg) as a solution in PEG 400 / 26% ethanol administered to healthy male subjects. Placebo controlled and blinded at each dose level
Investigator:	[redacted]
Study center(s):	Human Pharmacology Centre, Biberach
Publication (reference):	-
Clinical phase:	I
Objectives:	To assess safety, tolerability and pharmacokinetics of BIRB 1017 BS in single rising oral doses of 5 to 800 mg in a polyethylene glycol 400 (PEG 400) / 26% ethanol solution in healthy male subjects
Methodology:	Single rising dose, randomised, placebo controlled, double-blinded at each dose level
No. of subjects:	
planned:	48
actual:	48 (6 plus 2 placebo at each dose level)
Diagnosis and main criteria for inclusion:	Healthy, 18 to 50 year old male volunteers
Test product:	BIRB 1017 BS powder
dose:	5, 25, 100, 250, 500, and 800 mg dissolved in 20 mL PEG 400 / 26% ethanol
mode of admin.:	per os
batch no.:	B040047B
Duration of treatment:	Single dose
Reference therapy:	PEG 400
dose:	20 mL in 26% ethanol
mode of admin.:	per os
batch no.:	PD-2499 (PEG 400), 402454 (ethanol)
Criteria for evaluation:	
Efficacy:	Pharmacokinetics: plasma concentration time profiles of BIRB 1017 BS, pharmacokinetic parameters single dose (including C_{max}, $AUC_{0-\infty}$, t_{max}, $t_{1/2}$, CL/F, Vz/F, MRT)

Name of company: Boehringer Ingelheim		**Tabulated Study Report** **SUPPLEMENTARY SHEET**		
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Safety:	Adverse events, vital signs, laboratory values, 12 lead electrocardiogram, physical examination, tolerability
Statistical methods:	Descriptive statistics for safety and pharmacokinetics

SUMMARY – CONCLUSIONS:

Efficacy results:

Pharmacokinetics: Mean t_{max} values under fasting conditions were approximately 1 hour for all dose groups. Systemic exposure ($AUC_{0-\infty}$ and C_{max}) increased supra-proportionately to dose up to the 250 mg. Mean $AUC_{0-\infty}$ was approximately proportional to dose from 250 mg to 500 mg. The 800 mg exhibited a slight decrease in systemic exposure compared to 500 mg. Pharmacokinetics of BIRB 1017 BS exhibited moderately high inter-subject variability with CV values for $AUC_{0-\infty}$ mostly in the range 40% to 55%.

Safety results:

Dizziness was reported by six subjects each. Two subjects reported nasopharyngitis, two other suffered headache. One subject reported lymphadenopathy and another one diarrhoea. A causal relationship between the event and the trial drug was assumed by the investigator in five cases of dizziness, two headache and the diarrhoea. All subjects had fully recovered.

There was no evidence for a clinically relevant effect of BIRB 1017 BS on any ECG parameter. No relevant changes in morphology (including T waves and U waves), rhythm or conduction were observed. There was also no evidence for an impact on the QT interval.

Conclusions:

BIRB 1017 BS exhibited dose dependent pharmacokinetics with higher oral clearance at lower and high doses. Mean elimination half-life values were relatively similar, ranged approximately from 8 to 14 hours. Maximum attainable mean C_{max} was less than 900 ng/mL. 800 mg dose did not add to the exposure achieved with BIRB 1017 with the 500 mg dose topping out at ~ 900 ng/mL.

BIRB 1017 BS was safe and well tolerated in the given single doses of 5 mg up to 800 mg.