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: BIBT 1011		**Page:**	**Number:**	
Ref. to Documentation:	**Volume:** I	**Page:** to		**Addendum No.:**
Report date: 15 March 2002	**Number:** 1193.1	**Study period (years):** 2001		

Title of study:	Safety, pharmacodynamics, and pharmacokinetics after single oral administration of 1, 5, 10, 30, 100, 200 and 400 mg BIBT 1011 BS as drinking solution in healthy subjects. An open, placebo-controlled, randomised study, double blind at each dose level.
Investigator:	[redacted]
Study center(s):	Human Pharmacological Centre, BI Pharma KG Biberach
Publication (reference):	None
Clinical phase:	I
Objectives:	To assess safety, pharmacokinetics and the effect of BIBT 986 BS, given as BIBT 1011 BS, on coagulation parameters
Methodology:	Single rising dose, randomised, placebo controlled, blinded at each dose level
No. of subjects entered:	
total:	56
each treatment:	6 (BIBT 1011 BS) plus 2 (placebo)
Diagnosis and main criteria for inclusion:	Healthy male subjects, age 18 to 45 years, body mass index (BMI) ≥ 18.5 and ≤ 29.9 kg/m^2
Test product:	BIBT 1011 BS drinking solution
dose:	1, 5, 10, 30, 100, 200, 400 mg
mode of admin.:	per os (p.o.)
batch no.:	B010602, B010603, B010606, B010608, B010706, B010610, B010611, B010612, B010613, B010709
Duration of treatment:	Single dose
Reference therapy:	BIBT 1011 BS placebo drinking solution
dose:	-
mode of admin.:	p.o.
batch no.:	B010621, B010622, B010623, B010620, B010710, B010610, B010611, B010612, B010613, B010709

Name of company: Boehringer Ingelheim		**Tabulated Study Report**		**(For National Authority Use only)**
Name of finished product:		**SUPPLEMENTARY SHEET**		
Name of active ingredient: BIBT 1011		**Page:**	**Number:**	
Ref. to Documentation:	**Volume:** I	**Page: to**		**Addendum No.:**
Report date: 15 March 2002	**Number:** 1193.1	**Study period (years):** 2001		

Criteria for evaluation:

Efficacy: Primary endpoints: coagulation tests
Secondary endpoints: plasma concentration time profiles of BIBT 986, exploratory pharmacokinetics

Safety: Pulse rate, systolic and diastolic blood pressure (BP), electrocardiogram (ECG), routine laboratory , adverse events

Statistical methods: Descriptive statistics

SUMMARY - CONCLUSIONS:

Efficacy results: Quantifiable BIBT 986 BS plasma concentrations were not observed following administration of 1, 5 or 10 mg BIBT 1011. Following administration of 30 to 400 mg BIBT 1011 BS, BIBT 986 BS plasma concentrations increased in a dose-proportional manner.

Doses below 100 mg BIBT 1011 BS resulted in comparable pharmacodynamic activity to the placebo group. There was a dose-dependent increase in activity from 100 to 400 mg BIBT 1011 BS. For the blood coagulation parameters activated partial thromboplastin time (aPTT), international normalised ratio (INR) and ecarin clotting time (ECT), the maximal response was 1.5 – 2.5 times the baseline activity. For thrombin time (TZ), the maximal response was approximately 18 times the baseline activity. By 24 hr post-dose, the activity for all four endpoints had returned close to baseline.

For all four pharmacodynamic (PD) measurements, the relationship between BIBT 986 BS concentration and relative increase in baseline activity appeared to be reasonably linear.

Safety results: Three subjects reported headache. Two subjects felt dizzy or weak. All but headache in one subject were of mild intensity and completely recovered. None of the adverse events was regarded study drug related.

Conclusions: Single oral doses of up to 400 mg of BIBT 1011 BS were well tolerated. Plasma concentrations of BIBT 986 BS were measurable after administration of doses greater than 10 mg of the prodrug BIBT 1011 BS. Pharmacokinetic parameters AUC and C_{max} of BIBT 986 BS increased in proportion with dose. Dose dependent prolongations of blood coagulation times were observed.