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: BIIL 284 BS				
Name of active ingredient: [^{14}C]BIIL 284 BS		**Page:**	**Number:**	
Ref. to Documentation:	**Volume:**	**Page:**		**Addendum No.:**
Report date: 12th January 2001	**Number:**	**Study period:** 11-27 October 1999		

Title of study:	Investigation of Metabolism and Pharmacokinetics of [^{14}C]BIIL 284 BS After Administration of a Single Oral Dose of 25 mg [^{14}C]BIIL 284 BS in 6 Healthy Volunteers
Investigator:	[redacted]
Study center:	[redacted] Scotland
Publication (reference):	The study has not been published
Clinical phase:	I
Objectives:	The aims of this Phase I study are to define the metabolism, excretion and pharmacokinetics of [^{14}C]BIIL 284 BS after administration of a single oral dose of 25 mg [^{14}C]BIIL 284 BS in 6 healthy volunteers. Tolerability was also assessed
Methodology:	Open, non-randomised, radiolabelled single centre trial, involving 6 healthy male volunteers
No. of subjects entered:	
total:	6
each treatment:	6
Diagnosis and main criteria for inclusion:	Healthy male volunteers, age range from 30 to 55 years inclusive. Body weight between 50 and 100 kg and within 20% of ideal body weight (Metropolitan Life Assurance Company Tables 1983)
Test product:	[^{14}C]BIIL 284 BS
dose:	25 mg and *ca* 2 MBq
mode of admin.:	Oral
batch no.:	B990910
Duration of treatment:	One dose – 9 days monitoring and sample collection
Criteria for evaluation:	
Efficacy:	Not applicable – efficacy was not measured in this study
Pharmacokinetics:	Radioactivity concentrations in blood, plasma, urine and faeces; C_{max}, t_{max}, $t_{½}$, MRT, $AUC_{0-\infty}$, CL/f, V_d/f in plasma; excretion balance; $C_{blood\ cells}/C_{plasma}$ ratio; preliminary metabolite profiles in urine, faeces and plasma; BIIL 284 BS, BIIL 260 BS, BIIL 315 ZW, BIIL 304 ZW in plasma: C_{max}, t_{max}, $t_{½}$, MRT, $AUC_{0-\infty}$, CL/f, V_d/f

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Tolerability:	Adverse events
Safety:	Electrocardiograph (ECG), vital signs, clinical chemistry and haematology
Statistical methods:	Descriptive statistics

SUMMARY – CONCLUSIONS:

In plasma, BIIL 315 ZW was established as the main metabolite as it accounts for most of the radioactivity (derived from C_{max} and $AUC_{0-\infty}$). Parent compound BIIL 284 BS was not quantifiable in plasma. Additional metabolites BIIL 260 ZW and BIIL 304 ZW were detected only to a low degree in plasma. This suggests significant first pass metabolism of BIIL 284 BS following absorption from the gastrointestinal tract. All pharmacokinetic parameters of BIIL 315 ZW and radioactivity were highly variable but comparable to those obtained in the first single dose study. There was essentially no distribution of radioactivity into blood cells. The administered dose was quantitatively recovered over the duration of the study (192 h) with the main route of elimination via faeces (93% of dose). The majority of radioactivity was excreted between 24 h and 96 h after drug intake. Excretion was nearly complete after 96 h. The high amount of radioactivity found in the faeces is indicative of incomplete absorption of parent compound and/or biliary excretion of metabolites.

TABLE 1: Summary of pharmacokinetic parameters in plasma after administration of 25 mg [^{14}C]BIIL 284 BS as PSE solution in fasted state in healthy male volunteers (mean values of all parameters except t_{max}, which is given as median, %CV given in brackets)

Administration PSE solution, p.o., sd, fasted	N	Dose [mg]	t_{max} [h]	C_{max} [ng.ml^{-1}]	$AUC_{0-\infty}$ [ng.h.ml^{-1}]	MRT [h]	$t_{½}$ [h]
BIIL 315 ZW	6	25	1.25	30.6 *25.6 (64.8)	340 *285 (72.8)	15.3 (30.0)	20.8 (75.8)
Radioactivity	6	25	1.25	*25.8 (56.0)	*290 (49.0)	18.3 (38.5)	14.4 (40.6)

* [ng equiv.ml^{-1}]

Between 2-12% of the faecal radioactivity was chromatographically consistent with BIIL 284 BS. Faeces contained 2 major metabolites, each of which was more polar than parent. These components combined represented between 31.8 and 52.3% of dose. Urine samples (0-8 and 8-24 h) contained low levels of activity. The major metabolite present in the urine was more polar than parent and represented 0.2% of dose. Final metabolite identification is ongoing.

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Efficacy results:	Not applicable – efficacy not measured
Safety results:	There were no adverse events recorded during the study. There were no significant changes in clinical laboratory measurements, vital signs, physical findings or electrocardiograph's (ECG's) during the study.
Conclusions:	[^{14}C]BIIL 284 BS was tolerated well as a single oral dose of 25 mg when administered to six healthy male subjects.