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: ESR 1150 CL		**Page:**	**Number:**	
Ref. to Documentation:	**Volume:**	**Page:**	**to**	**Addendum No.:**
Report date: 19 September 2001	**Number:** U01-3294	**Study period (years):** 2 November 1998 to 16 December 1998		

Title of study:	Absolute bioavailability, pharmacokinetics and safety of ESR 1150 CL 1mg capsule compared to 0.015mg solution i.v. as single administration in healthy male subjects (open-labelled, 2-way cross-over study)	
Investigator:	[redacted]	
Study centre:	[redacted] Japan	
Publication (reference):	Not yet published	
Clinical phase:	I	
Objectives:	Absolute bioavailability, pharmacokinetics and safety	
Methodology:	Cross-over comparison of two treatment, open-labelled ,PK-measurement	
No. of subjects entered:		
total:	18 (8 subjects repeated the study and are counted twice)	
each treatment:	ESR 1150 CL p.o. - 9; ESR 1150 CL i.v. infusion - 9	
Diagnosis and main criteria for inclusion:	Healthy male volunteers, age 20 - 35 years, body weight 50 - 80 kg, Broca-index: ± 20 %	
Test product:	ESR 1150 CL capsule	ESR 1150 CL ampoule (0.02 mg as a hydrochloride)
dose:	1 mg as a hydrochloride	0.015 mg as a hydrochloride
mode of admin.:	per os	intravenous
batch no.:	98028	98027
Duration of treatment:	Single dose	
Reference therapy:	None	
dose:	not applicable	
mode of admin.:	not applicable	
batch no.:	not applicable	

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: ESR 1150 CL		**Page:**	**Number:**	
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Criteria for evaluation:

Efficacy:	Not applicable
Pharmacokinetics:	Bioavailability
Safety:	Adverse events, vital signs, laboratory tests

Statistical methods: Descriptive statistics

SUMMARY - CONCLUSIONS:

Efficacy results: Not applicable (In this pharmacokinetic study, there were no measures of efficacy.)

Pharmacokinetic results:
The absolute bioavailability of ESR 1150 CL after a single administration was evaluated through intraindividual comparison of $AUC_{0-\infty}$ in 8 subjects in each treatment. $AUC_{0-\infty}$ value after a single administration of 1 mg capsule and 0.015 mg i.v. solution were 838.0 ± 304.4 pg·hr/mL and 166.8 ± 38.9 pg·hr/mL, respectively. These values were normalized with respect to the dose, and the bioavailability was calculated. Bioavailability in humans was 7.89 ± 3.50% (range: 3.57 - 14.18%).

Safety results:
Twenty-four adverse events were observed in 5 of 18 subjects. None of them were serious adverse events. Seven adverse events in 4 subjects were judged as drug-related adverse events and all of them were observed in oral administration, and mild. All adverse events observed in intravenous administration were judged as non drug-related. Drug-related adverse events consisted of abdominal pain (x2), rigors (x2), dysuria (x2) and abdomen enlarged (x1)which might be due to the α-adrenoceptor agonistic effects, the major mechanism of action of ESR 1150 CL.
There were no drug-related abnormal changes in laboratory assessments, vital signs and ECG findings throughout this study.

Conclusions:
The absolute bioavailability of ESR 1150 CL after a single administration as evaluated through intraindividual comparison of $AUC_{0-\infty}$ in 8 subjects in each treatment, was 7.89 ± 3.50% (range: 3.75 - 14.18%).
Twenty-four adverse events were observed in 5 of 18 subjects. Seven drug-related adverse events in 4 subjects were observed in oral administration and they were mild. All adverse events observed in intravenous administration were judged as non drug-related.
The drug can be considered well tolerated in healthy male volunteers when administered as oral capsule 1 mg or as i.v. infusion 0.015mg for 5 min.