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: ALESION®				
Name of active ingredient: WAL 801 CL, Epinastine hydrochloride		**Page:**	**Number:**	
Ref. to Documentation:	**Volume:**	**Page:**		**Addendum No.:**
Report date: 28 December 2004	**Number:** U04-3556	**Study period (dates):** 23 June 2004 – 28 July 2004		

Title of study:	Bioequivalence of 20 mg of the new formulation of WAL 801 CL dry syrup compared to 20 mg of the conventional formulation of WAL 801 CL dry syrup following oral administration in healthy male volunteers (an open-label, randomised, single-dose, 2x2 crossover study)
Investigator:	[redacted]
Study center:	[redacted] [redacted] Japan
Publication (reference):	Data of this study has not been published.
Clinical phase:	I
Objectives:	To establish the bioequivalence of the new formulation of WAL 801 CL dry syrup vs. the conventional formulation of WAL 801 CL dry syrup
Methodology:	Open-label, randomised, single-dose, 2x2 crossover design
No. of subjects:	
planned:	entered: 34
actual:	enrolled: 34 (all subjects received both the new formulation of WAL 801 CL dry syrup and the conventional formulation) New formulation followed by conventional formulation: entered: 17 treated: 17 analysed (for PK and safety endpoints): 17 Conventional formulation followed by new formulation: entered: 17 treated: 17 analysed (for PK and safety endpoints): 17
Diagnosis and main criteria for inclusion:	Healthy male volunteers, age ≥ 20 and ≤ 35 years, BMI range: ≥ 18.5 and ≤ 25 kg/m^2
Test product:	WAL 801 CL dry syrup new formulation
dose:	20 mg (2.0 g as 1% dry syrup)
mode of admin.:	p.o.
batch no.:	B04067
Duration of treatment:	One day for each treatment
Reference therapy:	WAL 801 CL dry syrup conventional formulation
dose:	20 mg (2.0 g as 1% dry syrup)

Name of company: Boehringer Ingelheim		**Tabulated Study Report**		
Name of finished product: ALESION®		**SUPPLEMENTARY SHEET**		
Name of active ingredient: WAL 801 CL, Epinastine hydrochloride		**Page:**	**Number:**	
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mode of admin.:	p.o.
batch no.:	B04076
Criteria for evaluation:	
Pharmacokinetics:	Primary endpoints: AUC_{0-tz} and C_{max} Secondary endpoints: $AUC_{0-\infty}$, t_{max}, λ_z, $t_{1/2}$, MRT_{po}
Safety:	Physical examination, vital signs, laboratory tests and adverse events
Statistical methods:	Two-sided 90% CIs for the intra-subject ratio (as estimated by the geometric mean of the ratio) of AUC_{0-tz} and C_{max} were calculated to determine whether the CIs are contained in the acceptance range of 80-125% for bioequivalence. Additionally, the corresponding point estimators (geometric means) for the median intra-subject ratios were provided. The statistical model was ANOVA on log transformed parameters including effects for "sequence", "subjects nested within sequences", "period" and "treatment". The CIs were based on the residual error from ANOVA. Descriptive statistics for all other parameters were calculated. Frequencies were tabulated for all categorical parameters.
SUMMARY – CONCLUSIONS:	
Pharmacokinetic results:	The ratios of the adjusted mean values of C_{max} and AUC_{0-tz} of the new formulation to those of the conventional formulation were 0.854 and 0.826, respectively. The 90% confidence intervals (CIs) were from 78.4% to 93.0% for C_{max} and from 77.4% to 88.1% for AUC_{0-tz}, respectively. The lower limits of 90% CIs for C_{max} and AUC_{0-tz} were slightly outside of the acceptance range (80-125%), suggesting a lower bioavailability of the new formulation. Therefore, bioequivalence (BE) was not proven in this trial.
Safety results:	One subject experienced vasovagal reaction after administration of WAL 801 CL dry syrup conventional formulation. The intensity was mild and the event was judged not to be related to the study medication. The subject fully recovered. No other subjects reported adverse events.
Conclusions:	The results of this analysis did not meet the BE criteria, and thus bioequivalence between the new formulation and the conventional formulation was not proven in this trial. Single oral dose of 20 mg of WAL 801 CL dry syrup new formulation and the conventional formulation were well tolerated.