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: FLURINOL SYRUP®				
Name of active ingredient: Epinastine		**Page:**	**Number:**	
Ref. to Documentation:	**Volume:**	**Page:** **to**		**Addendum No.:**
Report date: 21 September 2000	**Number:**	**Study period (years):** 1998-1999		

Title of study:	A trial in Healthy Volunteers of the Relative Bioavailability of Epinastine Syrup, a New Galenic Form, compared to the Reference Product Tablets.
Investigator:	[redacted]
Study centre(s):	[redacted]
Publication (reference):	-
Clinical phase:	I
Objectives:	To assess the bioequivalence of two galenic formulations for epinastine (Flurinol®): syrup and 20 mg tablets.
Methodology:	Comparative, randomised, open label and crossover trial in healthy volunteers with an intermediate washout period of not less than one week. A trial including 24 healthy volunteers to evaluate the bioequivalence of two galenic formulations of Epinastine (200 mg/100 ml syrup and 20 mg tablets – reference formulation-) by means of 24 hours epinastine plasma concentration measurements in each volunteer receiving one and the other galenic form after 7 days of wash-out between both single dose administration.
No. of subjects entered:	24 healthy volunteers
total:	24
each treatment:	24
Diagnosis and main criteria for inclusion:	Healthy volunteers, between 21 and 45 years old, male or female, non-smokers, with normal blood and urine routine lab results, written informed consent.
Test product:	Epinastine syrup
dose:	20 mg (10 ml)
mode of admin.:	Oral
batch no.:	F4775
Duration of treatment:	One single dose of each formulation. Observation period: 24 h from treatment administration.
Reference therapy:	Epinastine tablets
dose:	20 mg
mode of admin.:	oral
batch no.:	L082107716

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Criteria for evaluation:

Efficacy: Twenty four hours plasma concentration measurements. Bioequivalence analysis with derived paremeters: area under the curve (AUC) epinastine plasma concentration versus time in 24 hours, peak plasma concentration (Cp_{max}), ratio Cp_{max}/AUC, time to peak (T_{max}), half-life ($T_{1/2}$).

Safety: Physical examination, vital signs, record of adverse events and withdrawals due to safety reasons.

Statistical methods: ANOVA tests for crossover design with three variants: subjects, treatments and periods. The individual values for each parameter, such as: area under the curve (AUC) Epinastine plasma concentration (Cp) versus time (24 hours), peak plasma concentration (Cp_{max}), time to peak (T_{max}), the ratio Cp_{max}/AUC and the drug half-life ($T_{1/2}$), were obtained by the PKCAL program. The statistical analyses was performed using the MKMODEL. In this trial was also included the transformed log of the Cp_{max}/AUC as an index of the absorption rate.
The bioequivalence analysis was performed by the Schuirmann D.J. Test and the Hauck W.W. and Anderson S. Test.

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SUMMARY - CONCLUSIONS:

Efficacy results:

Twenty four healthy volunteers (female/male = 9 / 15) were included. The 24 subjects completed an open label crossover study to compare bioavailability of Epinastine 20 mg tablets (reference formulation) with the syrup formulation at the same dose of 20 mg (10 ml = 20 mg). Peak plasma concentration is generally observed between 2 and 4 hours post dose. The relative Bioavailability of the syrup compared to the tablets went near to the unit. The observed serum half-life was of 5 hours for both formulations. For the kinetic parameter maximum plasma concentration (Cp_{max}), both formulations could be considered as equivalent within the 80% to 125% interval. For the area under the curve AUCt (linear trapezoidal model), the AUC_{∞} (area under the curve to time infinite) and the Cp_{max}/AUCt, a measurement for the absortion rate, the variability of these parameters for the reference formulation was greater than 50%. The ratios between both formulations, for AUCt, AUC_{∞} and Cp_{max}/AUCt, showed that both galenic formulations could be considered as equivalent within the interval 70% to 143%.

Safety results:

Twenty four volunteers were included in the safety analysis. There were not Serious Adverse Events (SAEs) or other significant adverse events during the trial. Two volunteers reported mild adverse events. One healthy volunteer reported migraine and another one somnolence. Both adverse events were considered as not related to trial medication, remission was recorded after 4 hours from onset. No concomitant medication was needed. No significant abnormal findings in vital signs or others were reported during the trial.

Conclusions:

The kinetic analysis for Epinastine syrup shows similar characteristic with that of the tablets.
For the maximum plasma concentration (Cp_{max}), both formulations can be considered as equivalent within the 80% to 125% interval. For the remaining kinetic parameters AUCt, AUC_{∞} and Cp_{max}/AUCt, a high variability was observed with the reference formulation. However, both formulations can be considered as equivalent for the interval 70% to 143% according to international guidelines for drugs with good therapeutic index, as is the case of Epinastine.

No drug related adverse event was observed, neither with the tablets nor with the suspension. Accordingly, both formulations resulted equally safe.