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 Trial Report**	Boehringer Ingelheim
Name of finished product: -		**EudraCT No.:** 2007-005293-31	
Name of active ingredient: Tamsulosin, Alna®		**Page:** 1 of 3	**Synopsis No.:**
Module:		**Volume:**	
Report date: 03 FEB 2009	**Trial No. / U No.:** 527.78 / U09-1124-01	**Date of trial:** 07 APR 2008 – 09 JUN 2008	**Date of revision** (if applicable)**:**

Title of trial:	An open label randomized two-way crossover study to investigate the effect of ketoconazole mediated CYP3A4 inhibition on the single oral dose pharmacokinetics of tamsulosin in healthy male volunteers (CYP2D6 extensive metabolizers).
Principal Investigator:	[redacted]
Trial sites:	Human Pharmacology Centre, Boehringer Ingelheim Pharma GmbH & Co. KG, Germany
Publication (reference):	None
Clinical phase:	I
Objectives:	To investigate the effect of CYP3A4 inhibition by ketoconazole on the single oral dose pharmacokinetics of tamsulosin and to investigate the effect on safety and tolerability
Methodology:	Open label randomized two-way crossover study in healthy male volunteers.
No. of subjects:	
Planned:	Entered: 24 (each treatment)
Actual:	Entered: 24 (each treatment) , Treated: 24, Analysed for primary endpoints: 24
Diagnosis and main criteria for inclusion:	Healthy male, age ≥ 21 and ≤ 50 years, BMI range: ≥ 18.5 and ≤ 29.9 kg/m^2
Trial product:	Tamsulosin (Alna®) 0.4 mg MR capsule and Ketoconazole
dose:	Tamsulosin: 0.4 mg q.d. on day 1 Ketoconazole: 400 mg q.d. on days -3 to 2
mode of admin.:	Oral administration with 240 mL water
batch no.:	not applicable
Reference therapy:	Tamsulosin 0.4 mg MR capsule
dose:	0.4 mg

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mode of admin.:	Oral administration with 240 mL water
batch no.:	not applicable
Duration of treatment:	Tamsulosin: 1 day for both treatments, separated by at least 14 days Ketoconazole: 5 days for the combination treatment
Criteria for evaluation:	Pharmacokinetics:
Efficacy / clinical pharmacology:	Primary endpoints: • Tamsulosin HCl pharmacokinetic parameters: C_{max} and $AUC_{0-\infty}$ Secondary endpoints: • Tamsulosin HCl pharmacokinetic parameters: AUC_{0-tz}, t_{max}, λ_z, $t_{1/2}$, MRT_{po}, CL/F, V_z/F • $RC_{max,T/R,}$ $RAUC_{0-\infty,T/R}$
Safety:	Physical examination, vital signs (BP and PR supine and standing), 12-lead ECG, laboratory tests, adverse events, assessment of tolerability by investigator
Statistical methods:	For the primary analyses, point estimators (geometric means) of the median intra-subject ratios of $AUC_{0-\infty}$, C_{max}, AUC_{0-tz} and their two-sided 90% confidence intervals (CIs) were derived. For the secondary analyses, descriptive statistics and tabular and graphical displays were used to summarize and evaluate the secondary endpoints.
SUMMARY – CONCLUSIONS:	
Efficacy / clinical pharmacology results:	Higher tamusulosin HCl exposure was seen in the subjects with 400 mg q.d. ketoconazole co-administration compared to the subjects with tamsulosin treatment alone: C_{max} and $AUC_{0-\infty}$ of tamsulosin HCl were increased by a factor of approximately 2.2 and 2.8, respectively. Co-administration of ketoconazole decreased the apparent clearance (CL/F) and the apparent volume of distribution (Vz/F) of tamsulosin HCl to approximately 35% and 40%, respectively. The terminal half life and the mean residence time of tamsulosin HCl with ketoconazole were slightly longer than those without ketoconazole co-administration. The median value of t_{max} was comparable between the two treatments.

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Safety results: Eight from 24 subjects experienced AEs during this study. All AEs were mild to moderate in intensity and fully reversible. The most frequent reported AEs were nasal congestion and headaches which were considered drug-related by the investigator. Headaches were mostly experienced under ketoconazole treatment, whereas nasal congestion occurred under co-administration of ketoconazole with tamsulosin HCl only. No AEs were experienced under treatment with tamsulosin HCl alone. No deaths and no serious AEs occurred. No findings of clinical laboratory parameters, vital signs, or ECG were considered clinically relevant. Tolerability was assessed as good in all subjects for all completed periods. Also, no orthostasis related AEs (e.g. blood pressure in standing versus supine position) or changes in blood pressure or pulse rate of clinical relevance were reported.

Conclusions: The co-administration of multiple oral doses of 400 mg ketoconazole to a single oral dose of 0.4 mg tamsulosin HCl was safe and well tolerated. Compared to the administration of tamsulosin HCl alone, there was no change in vital parameters like blood pressure and pulse rate of clinical significance. No orthostasis related AEs (e.g. blood pressure in standing versus supine position) were reported. However, C_{max} and $AUC_{0-\infty}$ of tamsulosin HCl increased approximately 2.2 fold and 2.8 fold with co-administration of ketoconazole. Therefore, tamsulosin HCl capsules should be used with caution in combination with moderate or strong inhibitors of CYP3A4 (e.g., ketoconazole), particularly at doses higher than 0.4 mg.