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: Bochringer Ingelheim		**Tabulated Study Report**		**(For National Authority Use only)**
Name of finished product: Ginsana® capsules				
Name of active ingredient: Standardised G115 Ginseng extract, adjusted to 4% ginsenosides		**Page:**	**Number:**	
Ref. to Documentation:	**Volume:**	**Page:** to		**Addendum No.:**
Report date: 31st October 2000	**Number:**	**Study period (years):** November 99 to April 00		

Title of study:	Efficacy of Ginsana® in improving half-time haemoglobin re-oxygenation in recreational sportspeople: a double-blind, placebo controlled pilot study
Investigator:	[redacted]
Study centre(s):	1
Publication (reference):	
Clinical phase:	II
Objectives:	To assess the efficacy of Ginsana® in improving half-time haemoglobin re-oxygenation in healthy, recreational sportspeople and to assess the safety of the product.
Methodology:	Randomised, double-blind, placebo-controlled, parallel group design according to international Good Clinical Practice (GCP)
No. of subjects entered:	
total:	26
each treatment:	Placebo 14; Ginsana® 12
Diagnosis and main criteria for inclusion:	Volunteer recreational athletes, aged 18 to 40, of either sex, who took part in physical activity of moderate intensity.
Test product:	Ginsana® capsules
dose:	1 x 100 mg capsule twice daily (b.i.d.) (200 mg/day)
mode of admin.:	Per os (p.o.)
batch no.:	828115
Duration of treatment:	12 weeks
Reference therapy:	Placebo
dose:	1 capsule b.i.d.
mode of admin.:	p.o.
batch no.:	835209

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Criteria for evaluation:

Efficacy:	**Primary Endpoint:** Baseline-adjusted change in half-time haemoglobin re-oxygenation as measured by the Near Infra Red Spectroscopy (NIRS) methodology at day 84
	Secondary Endpoints: Baseline-adjusted change in half-time haemoglobin re-oxygenation as measured by the NIRS methodology at days 21, 42 and 63
	Maximum endurance time and respiratory threshold
	Thiobarbituric acid (TBARS), Glutathione Superdismutase/Glutathione Superdismutase Oxidised (GSA/GSSG)
Safety:	Adverse event reporting, general clinical assessment at the start and end of the study; laboratory screen of haematology and blood chemistry
Statistical methods:	Descriptive statistics; t-tests of all the primary and secondary endpoints, Wilcoxon rank-sum tests where the assumptions of normality were not satisfied; Fisher's exact test for the global assessment of tolerability; tabulation of incidence, severity and causal relationship of all adverse events.

SUMMARY – CONCLUSIONS:

Efficacy results: At the baseline visit the mean values in the Intent-To-Treat population for half-time haemoglobin re-oxygenation were 25.6 and 26.9 seconds for the placebo and Ginsana® groups, respectively. At Day 84 the mean values were 26.2 and 27.3 seconds, respectively. The baseline-adjusted changes to Day 84 were decreases of 0.1 and 0.4 seconds, respectively.

The results indicated that there was a marginally greater mean improvement for the Ginsana® group (a reduction of 0.4 seconds) compared to the placebo group (a reduction of 0.1 seconds). The difference between the two groups was calculated as 0.29 seconds, with an associated 95% confidence interval of -4.23 to 4.80 seconds. The t-test showed that the difference between the two groups was not statistically significant (p-value of 0.896).

For the secondary variables tested, mean changes from baseline to Day 84 were marginally greater in the Ginsana® group, but only for the change in pre-exercise TBARS was the difference between Ginsana® and placebo statistically significant.

The change in half-time haemoglobin re-oxygenation for the Intent-To-Treat population in the placebo group showed an increase from baseline to Day 21 of 28.2 seconds, followed by steady decreases to days 42 and 63 of 27.4 and 26.8 seconds, respectively (followed by 26.2 seconds at Day 84 as described above). For the Ginsana® group there was an increase to 27.4 seconds at day 21, followed by a decrease to 26.5 seconds at day 63 and then a small increase to 26.8 seconds at Day 63 (rising to 27.3 seconds at Day 84 as described above). Performing t-tests to compare the two groups at each visit indicated that the differences between the two groups were not statistically significant.

The increase in mean respiratory threshold was greater in the Ginsana® group (0.05 compared to 0.03 in the placebo group) but the difference between the treatment groups was not statistically significant.

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When TBARS were compared between baseline and Day 84 the pre-exercise values for the placebo group had increased by a mean of 0.17, whereas for the Ginsana® group the decrease was 0.56. The estimated mean difference between the two groups was 0.74 and when a t-test was performed the difference was found to be statistically significant (p-value of 0.023).

The comparison between baseline and Day 84 for the post-exercise TBARS showed that the placebo group decreased slightly by 0.02. In the Ginsana® group the post exercise values had decreased by a mean of 0.62. The difference between the two groups was 0.60 in favour of Ginsana®, but a t-test showed that the difference was not statistically significant.

The Ginsana® group had a higher pre-exercise GSA/GSSG ratio by Day 84 compared to baseline, but this was not statistically significant in comparison with placebo.

The Ginsana® group always had a higher mean exercise duration than the placebo group. At baseline, the mean duration was just under 32 minutes for the Ginsana® group compared to just over 30 minutes for the placebo group. The Ginsana® group reported 31 minutes at Day 84 and the placebo group reported just under 30 minutes. However, there was no statistically significant difference in the time to maximum endurance achieved comparing the two treatment groups.

The Per-Protocol population results showed similar trends to the Intent-To-Treat population.

Safety results:

The mean duration of treatment was 79.8 days for the 14 subjects in the placebo group and 78.3 days for the 12 subjects in the Ginsana® group. Treatment compliance was calculated as good (<20% of the capsules returned) for all subjects in the placebo group and classified as good for all but 1 subject (whose treatment compliance was classified as moderate 20-30% of the capsules returned) in the Ginsana® group.

Adverse events were reported for 4 subjects in the placebo group (influenza-like symptoms (1 subject), sebaceous sacral cyst infection (1 subject) and pharyngitis (2 subjects)). Adverse events were reported for 5 subjects in the Ginsana® group (fever and arthralgia (knee pain) (1 subject), influenza-like symptoms (3 subjects) and an inflicted injury of a wrist sprain in the right hand (1 subject)).

With the exception of the influenza, which was reported by 3 subjects in the Ginsana® group compared to 1 subject in the placebo group, the few adverse events that occurred during the study were isolated events. None of the events were related to the product and there were no adverse events of severe intensity reported. Two of the influenza-like symptoms were of a moderate intensity, and all the other reported adverse events were of mild intensity. There were no serious adverse events, other significant adverse events or discontinuations for adverse events.

There were no clinically significant laboratory test findings, vital signs, physical examination findings or electrocardiogram findings.

In the global evaluation, treatment tolerability was rated good in both treatment groups by the subjects and by the investigator.

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Conclusions:

- The mean value for half-time haemoglobin re-oxygenation improved slightly more in the Ginsana® group (a decrease of 0.4 seconds) by day 84 compared to the placebo group (a decrease of 0.1 seconds), however the difference of 0.29 between the two groups was not statistically significant.
- Mean changes from baseline to Day 84 were marginally improved in the Ginsana® group for most of the secondary variables tested (maximum endurance time, respiratory threshold and perceived exertion using the Borg Scale). For the GSA/GSSG ratio the Ginsana® group showed a greater improvement from pre- to post-exercise for both Visit 1 and Visit 5. The analysis of the TBARS indicated that there was a slight improvement for the placebo group compared to the Ginsana® group. However, only for the change to Day 84 in pre-exercise TBARS was the difference between Ginsana® and placebo statistically significant.
- The few adverse events reported were of mild or moderate intensity and were not treatment-related. No serious adverse events were reported and there were no discontinuations for adverse events or other clinically significant adverse events or other safety findings.
- The treatments were well-tolerated.