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**		**(For National Authority Use only)**
Name of finished product: Aggrenox®				
Name of active ingredient: dipyridamole		**Page:**	**Number:**	
Ref. to Documentation:	**Volume:**	**Page: to**		**Addendum No.:**
Report date: 30 May 2001	**Number:** U01-3148	**Study period (years):** 11 October 2000 to 19 November 2000		

Title of study:	Comparison of pharmacokinetics of dipyridamole administered as Aggrenox® (dipyridamole extended release plus aspirin) capsule versus dipyridamole immediate release plus aspirin following alteration of stomach pH by the prior administration of a proton-pump inhibitor: An open-label 2-way randomized cross-over study in healthy male and female subjects age 40 - 65.
Investigator:	[redacted]
Study center(s):	[redacted] Canada
Publication (reference):	N/A
Clinical phase:	IV
Objectives:	Comparison of pharmacokinetics of dipyridamole administered as Aggrenox® versus dipyridamole administered as the immediate release formulation plus aspirin, under conditions of reduced stomach acidity.
Methodology:	Two-way cross-over, randomized, open-label trial.
No. of subjects entered: **total:** **each treatment:**	Thirty-one subjects were pre-treated with lansoprazole. Twenty-four of the 31 subjects were entered in and completed the study. All 24 subjects received both treatments (Aggrenox® and dipyridamole + aspirin). Of these, 20 subjects were evaluable for analysis of PK data.
Diagnosis and main criteria for inclusion:	Healthy female and male subjects 40 - 65 years old.
Test product:	Aggrenox®
Dose:	200 mg dipyridamole + 25 mg aspirin
Mode of admin.:	Oral
Lot no.:	006357
Duration of treatment:	Single dose
Reference therapy:	Dipyridamole immediate release (IR) + aspirin
Dose:	Dipyridamole 100 mg b.i.d. + aspirin 81 mg q.d.
Mode of admin.:	Oral
Lot no.:	302850003

Name of company: Boehringer Ingelheim		**Tabulated Study Report**		**(For National Authority Use only)**
Name of finished product: Aggrenox®		**SUPPLEMENTARY SHEET**		
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Criteria for evaluation:	
Efficacy:	N/A
Safety:	Adverse events and laboratory assessments
Statistical methods:	Analysis of variance and 95% confidence intervals for test / reference ratio of geometric mean AUC_{0-12h} and other PK parameters.

SUMMARY – CONCLUSIONS:

Efficacy results:

N/A Efficacy was not studied.

Pharmacokinetic results:

This study demonstrates that on average dipyridamole is about two times better absorbed from Aggrenox® than from the equivalent dose of the immediate release formulation of dipyridamole, when administered to individuals with reduced stomach acidity. Stomach pH was effectively elevated to pH values above 4.0 in all evaluable subjects by means of pretreatment for 5 days with the proton-pump inhibitor lansoprazole. Aggrenox® was administered as a single capsule of the commercially available drug, consisting of 200 mg extended-release dipyridamole plus 25 mg aspirin. Immediate release dipyridamole was administered in a manner intended to mimic a typical dosing regimen with generic dipyridamole and low-dose aspirin (two doses of 100 mg dipyridamole separated by 6 hrs, with 81 mg of aspirin administered with the first dose).

Safety results:

Aggrenox® and dipyridamole immediate release plus aspirin were generally well tolerated. All adverse events were either mild or moderate in intensity. There were no serious adverse events and no subjects discontinued the study due to adverse events.

There were no unexpected safety or tolerability results, as the adverse events with the highest incidence in this trial – headache, abdominal pain, nausea, diarrhea, and vomiting – were those frequently associated with Aggrenox®, dipyridamole immediate release, and aspirin. No new clinically important safety observations were noted.

Conclusions:

In conclusion, this cross-over comparison of the absorption of two formulations of dipyridamole demonstrates that the formulation in Aggrenox® (tartaric acid pellets), in contrast to a conventional immediate-release formulation, ensures reliable oral absorption of dipyridamole even under conditions of substantially reduced stomach acidity.