2 SYNOPSIS

Name of Sponsor/Company: Gedeon Richter Plc.	Individual Study Table Referring to Part of the Dossier Volume: Page:	(For National Authority Use Only)
Name of Product: Cavinton (10 mg Vinpocetine)		
Name of active ingredient: 10 mg Vinpocetine		

Study medication:
Aspirin Protect 100 mg tablet (containing 100 mg acetylsalicylic acid)
Cavinton injection (containing 10 mg vinpocetine)

Title of study:
Single center, exploratoric, open-label study to investigate the add-on effect of vinpocetine to the haemorheological effect of 100 mg acetyl-salicylicum in patients with chronic cerebrovascular disease

Principal Investigator and investigational site:
[redacted]
☎: [redacted]

Study period:	**Phase of development:**
Date of first enrolment: 20th April 2009 Date of last completed: 23rd June 2010	Phase 4

Objectives:

- To investigate the add-on effect of vinpocetine infusion to haemorheological effect of 100 mg acetylsalicylic acid in post-stroke patients.
- To investigate the safety and tolerability of co-administration of vinpocetine infusion and Aspirin Protect tablet.

Primary Endpoint: efficacy parameters:

- Haemorheological parameters: Platelet aggregation (determined using optical platelet aggregometer), Plasma fibrinogen, Haematocrit, Erythrocyte aggregation, Erythrocyte deformability, Full blood viscosity, Plasma viscosity
- Biomarkers: Soluble P-selectin, Von-Willebrand factor

Secondary Endpoints: safety parameters:

- Laboratory tests (haematology, biochemistry, urinalysis), ECG, Vital signs, Adverse events

Methodology:
Single center, one arm, open label clinical study.
Efficacy parameters, i.e. haemorheological parameters and inflammatory biomarkers were determined by enzyme-linked immunosorbent assay according to the protocol of the laboratory of the investigational site.

Number of patients (planned and analysed):
20 patients were enrolled and analysed in the study.

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Diagnosis and main criteria for inclusion:

- CT or MRI verified stroke due to large-vessel atherosclerosis according to TOAST criteria, which occurred more than 3 months before enrolment.
- Patient receiving 100 mg acetylsalicylic acid daily at least 1 month prior the enrollment, and the platelet inhibitor effect of acetylsalicylic acid is less than 40% (measured by optical aggregometry) at the screening.
- Age between 30 and 80 years (both males and females).
- 18 kg/m^2 ≤ BMI ≤ 35 kg/m^2 (and the minimal body weight is 40 kg)
- Signed Informed Consent.

Product, Dose And Mode Of Administration, Batch Number:

Name:	**Cavinton injection**
Formulation:	Injection
Manufacturer:	Gedeon Richter Plc. Budapest, Hungary
Active ingredient:	Vinpocetine
Unit dose:	10 mg vinpocetine
Mode of administration:	Parenteral, i.v. infusion
Regimen:	20, 30, 40, 50, 50, 50, 50 mg Cavinton injection into 500 ml saline solution
Batch number:	[redacted]
Expiry date:	[redacted]

Name:	Aspirin Protect 100 mg
Formulation:	Tablet
Manufacturer:	Bayer Hungaria
Active ingredient:	Acetylsalicylic acid
Unit dose:	100 mg acetylsalicylic acid
Mode of administration:	Oral
Regimen:	1 tablet daily, after meal
Batch number:	[redacted]
Expiry date:	[redacted]

All patient received 1 tablet of Aspirin 100 tablet (containing: 100 mg acetylsalicylic acid) daily, after meals, and vinpocetine infusion in escalating dose in the following manner: 20, 30, 40, 50, 50, 50, 50 mg vinpocetine injection per day into 500 ml saline solution. The rate of infusion was 60 drops/min.

Duration of treatment:
Each patient was treated for 1 week.

Criteria for evaluation:

Efficacy:
Efficacy parameters (haemorheological parameters and biomarkers) were assessed at predefined time points throughout the study.
Safety:
Medical history, physical examination, laboratory safety tests, vital signs, 12-lead electrocardiograms (ECGs) were assessed at predefined time points throughout the study.

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Reference Therapy, Dose and Mode of Administration, Batch Number:
Not applicable, no reference therapy was administered in the study

Statistical methods:

Efficacy parameters:

Analysis was performed on the ITT/PP sets.

Descriptive statistics is presented for all efficacy parameters.

The values from baseline and Visit 2 and Follow-up and the value between two consecutive visits were analysed by ANOVA and post hoc analysis was performed to compare the corresponding visits.

Safety parameters:

Analysis was performed on the safety set. No AEs were reported, therefore coding by Medical Dictionary for Regulatory Activities (MedDRA) was unnecessary. Medical history updates, vital signs, physical examination results, laboratory safety tests and ECG parameters are summarised using descriptive statistics. Shift tables showing changes from baseline were generated, where appropriate. The clinical relevance of 12-lead ECG findings was also indicated in data listings.

Summary - Conclusions

Efficacy Results:

Results showed a statistically significant ($p<0.05$) improvement in the level of Von-Willebrand factor by the end of treatment compared to baseline that was maintained up to follow-up (7 days after end of treatment). Regarding erythrocyte deformability, a trend ($p<0.1$) towards improvement by the end of treatment compared to baseline could be observed. The change from baseline in no other parameters reached any notable difference.

Safety Results:

No adverse events were reported throughout the study. No safety lab assessment results deemed clinically significant as per the judgement of the investigator. In vital signs, no clinically significant changes were observed.

Regarding 12-lead ECG, prolongation of QTcB interval with >30ms at any post baseline time point compared to baseline was observed in 6 patients (30%), out of whom 2 patients (10%) experienced QTcB prolongation of >60ms. 2 patients with QTcB less than 450 ms at baseline reached post-baseline values of 450-480 ms.

Conclusion:

Based on the results no firm conclusion can be drawn on whether vinpocetine may have a beneficial effect in improving Aspirin resistance in patients with cerebrovascular disease.

Regarding safety, no adverse events were reported throughout the study. Neither safety lab assessment results nor vital sign measurement results deemed clinically significant. Prolongation of QTcB interval was noted in several patients.

The study did not reveal any new safety information that would indicate a change of the currently known safety profile of Cavinton.

Date of the report:
9 October 2018