2 SYNOPSIS

Name of Sponsor/Company: Pierre Fabre Medicament	*Individual Study Table referring to Part of the Dossier*	*(For National Authority Use only)*
Name of Finished Product: Not applicable.	*Volume:*	
Name of Active Ingredient: Alprostadil 0.4 %	*Page:*	

Title of study:

A phase II double-blind vehicle-controlled crossover single dose (400 µg) V0147 gel effect and tolerance study in spinal cord injured patients with erectile dysfunction.

Protocol number: V00147 GL 202 **SGS Aster Reference:** P070112

Principal Investigator:

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Study period:			**Drug Development Phase:**
First subject first visit	:	June 04th, 2007	Phase II
Last subject last visit	:	July 25th, 2007	

Objectives:

Primary objective:
The main objective of the study was to assess the ability of a single dose of 400 µg V0147 gel versus vehicle applied locally to induce an erectile response in spinal cord injured patients with erectile dysfunction.

Secondary objective:
The secondary objective was to assess the local and general tolerability of V0147 gel.

Methodology:

Pilot, double-blind, vehicle-controlled, crossover, single dose study in spinal cord injured patients with erectile dysfunction.

Number of subjects (planned and analysed):

Planned	:	24	Completed the trial	:	15
Screened/enrolled	:	15	In safety analysis	:	15
Included	:	15			

Diagnosis and main criteria for inclusion:

The study was planned to be carried out in 24 male volunteers with spinal cord injured assessed by the American Spinal Injury Association (ASIA) scale, aged 18 to 40 years old and with a body mass index (BMI) between 18 and 32 kg/m^2.

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Duration of treatment:

One single dose of V0147GL gel and vehicle separated by 1 week between the two dose applications.

Test product, dose and mode of administration, batch number:

Product and Formulation:	Alprostadil gel (V0147GL)
Batch number:	CLP066
Expiry or retest date:	09/2007
Mode of administration:	Local
Dosage/regimen:	400-µg single dose

Reference/Comparator product, dose and mode of administration, batch number:

Product and Formulation:	Vehicle gel
Batch number:	CLP064
Expiry or retest date:	09/2007
Mode of administration:	Local
Dosage/regimen:	400-µg single dose

Criteria for evaluation:

Efficacy:

- Penile response evaluated with an Erection Assessment 5 point scale

- 1 = no response (flaccidity),
- 2 = some enlargement (not likely to be sufficient for penetration)
- 3 = full enlargement (but insufficient rigidity),
- 4 = erection sufficient for vaginal penetration but not fully rigid
- 5 = full rigidity

The response was evaluated by the Investigator.

The evaluation was made immediately before the administration of each topical formulation dose and 15, 30, 45 and 60 minutes thereafter.

Before the application of the product the penile response score was at 1 (score = 1 as flaccidity) on the Erection Assessment Scale.

- Percentage of patients with an improvement of at least 3 points as compared to the baseline (score = 1 as flaccidity) on the Erection Assessment Scale.

- Latency and duration of the response:

- mean time to onset of response (min)
- mean time to maximal response (min)
- mean time to return to non-erect state (min)

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Criteria for evaluation (continued):

Tolerance:

- Vital signs at pre-selection, before and 15, 30, 45, 60 minutes after V0147GL gel and vehicle dose application,
- Local and Global safety (adverse events) at each visit,
- Local tolerance by assessment at each visit: erythema and/or burning sensation and/or pain on the following 4-point scale:
  - 0 = none
  - 1 = mild
  - 2 = moderate
  - 3 = severe

Statistical methods:

The main criterion was the binary variable (yes/no) indicating that the patient reaches the grade 4 on the Erection assessment 5-point scale. Parametric approach based on GEE equations for repeated measures was used to provide an estimate of the treatment effect and the significance of the test that there is no difference between treatments. The model accounted for the factors period, treatment and patient. Carry-over effect was tested as well. Significance level of the tests was set to 0.05.

The Penile response evaluated with an Erection Assessment 5 point scale was tested using a non-parametric approach for cross-over designs.

Criteria for latency and duration of the response were analysed using an analysis of variance involving the random patient factor. These criteria included:

- mean time to onset of response (min)
- mean time to maximal response (min)
- mean time to return to non-erect state (min)

The local tolerance assessment of erythema, burning sensation and pain were described at each visit.

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Results:

Efficacy:

The penile response was slightly improved 15 minutes after application of alprostadil gel for 2 patients only; one of them had a score at 4 and the other one a score at 5. For other patients the score remained at 1 or 2 as well as for patients receiving placebo application. Before application and 30 minutes after application, the score remained at 1 or 2 for all patients whatever the gel applied.

Only 2 patients reported an improvement of at least 3 points of their penile response after alprostadil gel application.

Concerning latency and duration of response, there was no significant difference between alprostadil and placebo.

In summary, under the conditions of this study, alprostadil did not show a better efficacy than placebo.

Further to this lack of efficacy, the study was prematurely discontinued.

Safety:

A total of 2 adverse events were reported by 2 subjects, none of them was either serious, or severe. Both adverse events were considered as unrelated to treatment application.

Neither trends nor relevant changes from baseline were observed in vital signs parameters and physical examinations.

Local tolerance was good for all patients.

In summary, a single dose of 400 µg V0147 gel was safe and well tolerated.

Conclusions:

This study has shown that:

- Under the conditions of this study, alprostadil did not show a better efficacy than placebo. This lack of efficacy has lead to interruption of the study and of the development of alprostadil.
- A total of 2 adverse events were reported by 2 subjects, none of them was either serious, or severe. Both adverse events were considered as unrelated to treatment application.
- Neither trends nor relevant changes from baseline were observed in vital signs parameters and physical examinations. Local tolerance was good for all patients.
- In summary, a single dose of 400 µg V0147 gel was safe and well tolerated.

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