Pierre Fabre Médicament
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1. TITLE PAGE

CLINICAL STUDY REPORT

Evaluation du pouvoir bactériostatique de la préparation V0079 CETAVLON® sur la flore cutanée au niveau des mains. Etude preuve de concept.

Investigational product: V0079CR

Protocol number: V00079CR402

Phase of development: phase IV

EudraCT number: 2007-005921-31

Date of first enrolment: Octobre 2008

Date of last completed: Novembre 2008

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Date of report: Novembre 2009
Study performed in compliance with Good Clinical Practice.

1. SYNOPSIS

Name of Company: Pierre Fabre Médicament	**Individual Study Table**	**(For National Authority Use Only)**
Name of finished product: Cetavlon	**Referring to Module 5 of the Dossier**	
Name of active substance *(or ingredient)***: Cetrimide**	**Vol.: .....Page: .....**	

Title of study:	Evaluation of the bacteriostatic effect of preparation V0079 CETAVLON® on the cutaneous flora of the hands. Proof-of-concept study.	
Investigators:	Christine Saint-Martory Hôtel Dieu 2, rue Viguerie 31025 Toulouse Cedex 3 Jennifer Theunis Hôtel Dieu 2, rue Viguerie 31025 Toulouse Cedex 3	
Study centre(s):	Skin Research Institute – Pierre Fabre Research Institute Hôtel Dieu, Clinical Pharmacology Unit 2 Rue Viguerie, BP 3071 31025 Toulouse Cedex 3	
Publication (reference):	/	
Studied period *(years, months)***:** **Date of first enrolment:** **Date of last completed:**	 October 2008 November 2008	**Phase of development:** Phase IV
Objectives: **Primary:**	Evaluate the change in cutaneous flora after use of preparation V0079CR on the hands by microbiological measurements (count and identification).	
Secondary:	Document local clinical tolerance.	
Methodology:	Analysis of the cutaneous flora of the hands, in an open-label, randomised, controlateral study on 30 healthy volunteers. After randomisation, a sample of the cutaneous flora of the hand (control) was taken, followed by application of the product to the other hand, with samples taken after 5 and 60 minutes. The test took account of the following bacterial groups: aerobic, anaerobic, Gram +, Gram -, bacilli, cocci.	
Number of patients (planned and analysed):	28 expected, 24 included. Analysed: FAS: 24, PP: 22 and Tolerance: 24.	
Diagnosis and main criteria for inclusion:	Male or female subjects, age 18 to 65. Women of childbearing age: effective contraception, started at least 3 months earlier, continued during the study and for one month after the end of the study (intra-uterine device, pill, cutaneous implant, tubal ligation). Subject with French health insurance cover up until at least one month after the end of the study, or with equivalent cover. Subject considered to be clinically healthy by the investigator, after medical questionnaire and a physical examination, and sufficiently cooperative to be able to comply with the study requirements. Registration on the national biomedical research subject register. Subject having given their written consent to participate in the study.	

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Test product, **Dose,** **Mode of administration,** **Batch number:**	V0079CR Single-dose, on one hand. Topical application.
Other product, **Dose,** **Mode of administration,** **Batch number:**	NA
Duration of treatment:	Single-application.
Reference therapy, **Dose,** **Mode of administration,** **Batch number:**	NA
Criteria for evaluation: **Efficacy:**	Primary endpoint: Change in biomass on the treated hand 5 minutes after application, compared to the control hand; Secondary endpoints: Evaluation of product remanence 60 minutes after application (compared to T = 5 min); Evaluation of the change in biomass 60 minutes after product application (compared to the control); Biomass description ('control' hand, treated hand, T = 5 min and treated hand T = 60min).
Safety:	Local and overall tolerance assessment.
Statistical methods:	All statistical tests were expressed bilaterally with a level of significance of α=5%. The main analysis was performed on the FAS (Full Analysis Set) population. The analysis on the Per Protocol (PP) population was secondary. The primary endpoint consists of comparing, before (T0) and after (T5min) product application, the biomass on the hand. H0: No significant difference between the means at the two intervals. H1: There is a significant difference between the means at the two intervals. Secondary endpoints Product remanence at T60 min compared to T5min was evaluated on the individual difference in the cutaneous flora between T60min and T5 min on the treated hand. The change in biomass 60 minutes after product application was evaluated compared to the control hand, on the individual difference in flora atT60 min on the treated hand and the control hand. According to the type of distribution of the series of differences between the control and T=5min, the paired Student or Wilcoxon test was performed on the raw values and/or the logarithms.

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Tolerance was assessed by the investigator at T=60 min based on the following score:
1 = Very good tolerance_no functional signs of discomfort and no objective signs during the examination.
2 = Good tolerance _ some minor and temporary functional signs of discomfort not having led to discontinuation of application or objective signs during the examination.
3 = Average tolerance _ clear or persistent functional signs of discomfort or objective signs during the examination not having led to discontinuation of application of the investigational product.
4 = Poor tolerance_functional signs and/or objective signs leading to discontinuation of the investigational product.
The results were expressed as frequencies and percentages.

Summary – Conclusions:

24 subjects were included. 54.17% of women, average age 53.10 (min 23.19–max.64.15). The statistical analysis of the microbiological results shows a significant reduction in aerobic-anaerobic cutaneous flora between T0-T5 and T0-T60 (mainly seen by cocci and Gram+ bacilli), and aerobic flora (Gram+ cocci). At T60, gradual recolonisation is noted and revealed to be significant, especially in the most highly representative group (Gram+ cocci). The important point to be emphasised however is flora remanence (difference T0-T60) and balance. Local tolerance is very good in 100% of cases.

Conclusion

This study demonstrated immediate and significant antimicrobial activity from the treatment V0079CR (T5) and an effect after 60 minutes with no risk of dysmicrobism (T60).