Pierre Fabre Dermo-cosmétique

Represented by: Institut de Recherche Pierre Fabre

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1. TITLE PAGE

CLINICAL STUDY REPORT

NON-INFERIORITY STUDY OF A MALATHION 0.5% LOTION VERSUS REFERENCE THERAPY IN THE TREATMENT OF HEAD LICE: MULTICENTRE, RANDOMISED, INVESTIGATOR MASKED, PARALLEL GROUP

Investigational product: V3777 A / malathion 0.5% lotion

Study Design: International multicentre, randomised, blind assessment, phase III study, on two parallel groups "V3777 A" lotion versus reference therapy Prioderm® lotion

Protocol number: V03777 LE 301 A

Phase of development: III

Date of first enrolment: 24/11/2008

Date of last completed: 02/11/2009

Co-ordinator(s): Pr O. CHOSIDOW, olivier.chosidow@hmn.aphp.fr

Sponsor Representative(s) for study report:

Clinical Monitor (Mrs Myriam CONDOMINES, myriam.condomines@pierre-fabre.com),

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Medical Study Manager (Mr Nabil SAÏCHI, nabil.saichi@pierre-fabre.com)

Date of Report: 07 September 2010

Study performed in compliance with Good Clinical Practice.

2. SYNOPSIS

Name of Company: Pierre Fabre Médicament	**Individual Study Table**	**(For National Authority Use Only)**
Name of finished product:	**Referring to Module 5 of the Dossier**	
Name of active substance *(or ingredient)***:** **Malathion**	**Vol.: .....Page: .....**	
Title of study:	Non-inferiority study of a malathion 0.5% lotion versus reference therapy in the treatment of head lice: multicentre, randomised, investigator masked, parallel group.	
Investigators:	PI: Pr Olivier CHOSIDOW	
Study centre(s):	Belgium, France, Romania, Italy, Estonia.	
Publication (reference):		
Studied period *(years, months …)***:** **(date of first enrolment)** **(date of last completed)**	First enrolment in November 2008 & last enrolment in November 2009	**Phase of development:** III
Objectives: **Primary:**	To assess the non-inferiority of malathion 0.5% lotion (V3777 A) versus Prioderm® lotion (0.5% malathion), in the cure of the head lice 14 days after the first application. The cure was defined by the absence of live lice.	
Secondary:	- To assess the head lice infestation, 2 days after one single application of the lotion, - To assess the local and general tolerability of the lotions, - To assess the cosmetic acceptability of the two lotions.	
Methodology:	International multicentre, cluster randomised, blind assessment, phase III study, on two parallel groups "V3777 A" lotion (0.5% malathion) versus reference therapy Prioderm® lotion (0.5% malathion).	
Number of patients (planned and analysed):	495 patients	
Diagnosis and main criteria for inclusion:	**Inclusion criteria**: were eligible patients who met the following criteria: - patients aged 2 years or more, - confirmed active head lice infestation, with at least 5 live lice on the half-head (adult lice and nymphs), - patients accepting not to use any product in the same indication during the study period,	

Test product, **Dose,** **Mode of administration,** **Batch number:**	***"V3777 A" lotion (Malathion 0,5%); flask of 110 mL*** one single application of the lotion on the scalp and dry hair. Topical CLP077
Duration of treatment:	Two applications performed on day 0 (D0), and on day 10 (D10).
Reference therapy, **Dose,** **Mode of administration,** **Batch number:**	**Prioderm®** ***lotion (malathion 0.5%); flask of 110 mL*** 10 to 20 mL Topical 071596, 081602, 082589
Criteria for evaluation:	
Efficacy:	**Primary criterion** - cure rate of head lice 14 days after the first application of the lotion; this criterion was assessed by the rate of patients without live lice on day 14 (D14). **Secondary criteria** - the rate of patients without live lice 2 days (D2) after one single application of the lotion, - assessment of the cosmetic product acceptability by a 4-point scale (very satisfactory, satisfactory, not very satisfactory, not at all satisfactory) on Day 0 (D0).
Safety:	- Assessment of the local and general safety (adverse events), - Local tolerance by assessment at visit 1 and visit 3 : stinging and/or itching and/or paraesthesia and/or drying of the scalp, on the following 4-point scale: 0 = none 1 = mild 2 = moderate 3 = severe
Statistical methods:	The primary efficacy criterion was the response to treatments, defined by the absence of live head lice 14 days after the first application of the lotion. The 95% confidence interval of the difference of success rates between test and reference drugs was estimated taking into account the cluster (household) randomisation. If the lower bound of this confidence interval was higher than -10%, the test drug was declared non inferior to the reference drug.

Summary - Conclusions:

Efficacy results

On day 14, response to treatment was high in both groups: 83.7% in the V3777A group and 90% in the Prioderm® group in ITT as randomised population.

The difference of the response rate (V3777A - Prioderm®) was -6.3%. The low limit of the standard 95% confidence interval calculated for this difference ([-13.8%;1.2%]) was lower than -10% (non-inferiority limit: -10%).

The non-inferiority between the V3777A group and the Prioderm® group, measured by the success rate on day 14 was not concluded. The results obtained in other populations gave to the same conclusion.

On day 2, response rate was also high in both goups in ITT as treated population (89.7% in V3777A group and 90.9% in Prioderm® group). The difference of the response rate (V3777A - Prioderm®) was -1.3% (95% CI: [-7.7%;5.2%]).

Assessment of the cosmetic acceptability of the test products, assessed both by the study personnel and by the patients (or their parents or guardians), showed statistically significant differences in favour to V3777A lotion. The study personnel rated the V3777A lotion more highly for its ease of application, texture, odour and the overall agreement. This favourable appreciation was confirmed by the subjects who gave preference to V3777A lotion with regard to its odour, ease of elimination during hair washing and the condition of the hair after washing and drying. The profile of acceptability of the V3777 A lotion was therefore better than that of Prioderm®.

Safety results

The safety profile of the V3777A lotion was at least as good as that of Prioderm®.

-Twice as many adverse events in the Prioderm® group (most frequently reported adverse event: pain)

- One patient in each group experienced an adverse event leading to definite study treatment discontinuation (for which the relationship to the study treatment was not excluded).
- The study of local tolerance showed a similar profile for both products, AEs limited to mild manifestations such as stinging and itching.

Conclusion

With regard to the primary efficacy endpoint, the response to treatment was high in both groups, reaching 83.7% in the V3777A group and 90% in the Prioderm® group in the ITT 'as randomised' population. However, V3777A lotion did not meet the criteria for non-inferiority to Prioderm®. The profile of acceptability of the V3777A lotion and its safety profile were better those that of Prioderm®.

Overall, V3777 A lotion, with a reduced duration of application of one hour, showed a high success rate but did not demonstrate an efficacy equivalent to that of Prioderm® lotion applied for 8 hours, although it improved convenience of use and cosmetic acceptability compared to this reference product, which may confer an advantage as regards compliance with treatment.

Date of report 07 September 2009