OFFICE OF CLINICAL PHARMACOLOGY REVIEW

NDA: 022408/S005	Submission Date(s): 3/4/2014
Brand Name	Natroba Topical Suspension, 0.9%
Generic Name	Spinosad
Primary Reviewer	Doanh Tran, Ph.D.
Secondary Reviewer	Capt. E. Dennis Bashaw, Pharm.D.
OCP Division	Division of Clinical Pharmacology 3
OND division	Division of Dermatology and Dental Products
Sponsor	ParaPro
Submission Type	Efficacy supplement
Formulation; Strength(s)	Topical suspension, 0.9%
Indication	Topical treatment of head lice infestations in patients 6 months of age and older.

Background:
NDA 22408 for Natroba (spinosad) Topical Suspension, 0.9% was approved on January 18, 2011 for the topical treatment of head lice infestation in patients 4 years of age and older. The approval letter included the following Pediatric Research Equity Act (PREA) postmarketing requirement:

> A pharmacokinetic and safety study in pediatric patients ages 6 months to 4 years of age with active head lice infestation. This study should be conducted under maximum use conditions and include a minimum of 24 evaluable patients who will undergo pharmacokinetic sampling and assessments of local and systemic safety at appropriate time points.

The sponsor has completed a pharmacokinetic (PK) trial SPN-109-11 to fulfill the PREA postmarketing requirement. The sponsor previously submitted the results of this trial to NDA 022408 under supporting document number (SDN) 88 on 5/29/2012. The results from trial SPN-109-11 were reviewed in Clinical Pharmacology review by this reviewer dated 3/25/2013 with the recommendation that the trial results were acceptable to fulfill the PREA postmarketing requirement stated in the approval letter dated 1/18/2011. Please see this prior review for details of trial SPN-109-11.

Current submission:
The sponsor is submitting an efficacy supplement referencing the results of trial SPN-109-11 submitted under SDN 88 and requests that the indication be modified to include patients 6 months to 4 years of age. The sponsor also proposes to update the PK section of the label with new information from trial SPN-109-11.

Recommendation:
The Office of Clinical Pharmacology/Division of Clinical Pharmacology 3 has reviewed NDA 022408/S005 and finds it acceptable pending agreement on labeling revisions. In addition, the results of trial SPN-109-11 are considered acceptable to fulfill the PREA postmarketing requirement stated in the approval letter dated 1/18/2011.

We have the following recommended labeling revisions to section 12.3 of the proposed label. Deletion are noted as ~~strikethrough~~ and additions are noted as double underlines.

12.3 Pharmacokinetics

An open-label, single-center (b) (4) -trial was conducted over a period of seven days to determine the pharmacokinetic profile of spinosad 1.8% in pediatric subjects with head lice infestation. Fourteen (14) subjects, 4 – 15 years of age, with head lice were enrolled into the (b) (4) trial. All subjects applied a single topical (scalp) treatment of spinosad 1.8% for 10 minutes, after which the test article was washed off, and subjects underwent plasma sampling. (b) (4) Results demonstrated that spinosad was below the limit of quantitation (3ng/mL) in all samples. Plasma concentration of benzyl alcohol was not determined in these subjects.

An open-label, two-center (b) (4) -trial was conducted over a period of 23 days to determine the pharmacokinetic profile of spinosad 0.9% and the ingredient benzyl alcohol in pediatric subjects with a head lice infestation. Twenty-six (26) subjects between 6 months to 4 years of age were enrolled into the study per protocol. All subjects applied a single topical (scalp) treatment of spinosad 0.9% for 10 minutes, after which the test article was washed off, and subjects underwent plasma sampling over a 12 hour period (b) (4) -Plasma spinosad concentrations were below the limit of quantitation (3 ng/mL) in all samples.

(b) (4) Benzyl alcohol was (b) (4) quantifiable (above 1 µg/mL) in a total of 8 plasma samples in 6 out of 26 subjects (25%): four out of 12 subjects in the 6 months to <2 years age group and two out of 14 subjects in the 2 to 4 years age group. The highest observed concentration was 2.37 µg/mL. Benzyl alcohol concentrations at 12 hours post-treatment were below limit of quantification (1 µg/mL) for all subjects (b) (4)

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/s/

DOANH C TRAN
09/18/2014

EDWARD D BASHAW
09/19/2014