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A COMPREHENSIVE REVIEW: COMPLETE CHEMICAL DRUG PROFILE OF A DRUG ABAMETAPIR LOTION FOR HEAD LICE TREATMENT INCUDING CLINICAL STUDY EVALUATION.

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ABSTRACT:

Few therapies are effective in treating all stages of the life cycle of head lice (Pediculus capitis), which continue to be a common problem, especially in youngsters. By chelating vital metal cofactors, the metalloproteinase inhibitor abametapir interferes with lice's ability to make eggs and survive. Rapid absorption and conversion to a persistent carboxyl metabolite are demonstrated by pharmacokinetic studies. A single 10-minute application of abametapir 0.74% lotion resulted in significantly higher cure rates compared to the vehicle (81–82% vs. 47–51%, $p < 0.001$) in two phase III randomized controlled trials (NCT02060903, NCT02062060), with rapid louse elimination observed as early as day 1. Laboratory studies confirmed complete ovicidal activity across all stages of egg development. Only minor, temporary cutaneous responses were noted, indicating that the therapy was well tolerated.With its single-dose efficacy, ovicidal action, and favorable safety profile, abametapir represents a significant breakthrough in the treatment of pediculosis and is a good first-line treatment for head lice infestation.

Keywords: Abametapir 0.74% (Xeglyze), Head lice infestation, Pharmacology/efficacy, Ovicidal activity, Clinical trials (Phase II & Phase III), Adverse events.

1.Introduction:

Head lice is the most prevalent in children aged 5 to 11 years and in girls, while being uncommon among individuals of African descent [5]. Head lice (Pediculus capitis) are common human ectoparasites, most frequently affecting school-aged children. Successful treatment of an infestation requires targeting all stages of the approximately 30-day life cycle, including eggs, nymphs, and adults. Louse eggs are attached to the hair shaft, usually within 1.5 cm of the scalp, and typically hatch between 7 and 12 days after being laid [2].

The nymph stage lasts approximately 6 to 12 days, after which lice mature into adults capable of reproduction. An adult female typically lays 4 to 5 eggs per day over a span of about 16 days. Few treatments directly target the egg stage of the life cycle, and even those claiming ovicidal activity have not shown complete effectiveness. For this reason, most therapies recommend a second application 7 to 14 days after the initial dose to eliminate lice that may have hatched from eggs present during the first treatment. This approach applies to commonly used over-the-counter products, which contain synergized pyrethrins or synthetic pyrethroid insecticides such as permethrin. Among currently available prescription options, malathion lotion is the only one with published evidence supporting direct ovicidal activity [2].

Abametapir is a metalloproteinase inhibitor that disrupts enzymes essential for lice development and egg hatching. Its effectiveness in treating head lice infestations has been demonstrated in two phase 3 clinical trials. In these studies, a 0.74% abametapir lotion was applied to dry hair for 10 minutes, and a single treatment successfully eradicated lice in over 80% of participants. To evaluate its clinical ovicidal activity, louse eggs are typically treated while still on the host's scalp, then collected and incubated under conditions favorable for hatching. Comparing pre- and post-treatment eggs enables precise measurement of hatch rates between treated and untreated eggs from the same individual [2].

Further studies conducted on body louse eggs showed that abametapir exhibited complete (100%) ovicidal activity across all egg stages. Since ovicidal efficacy is a key element of successful louse-control therapies, these findings provide clear evidence that abametapir is capable of preventing the hatching of both head and body louse eggs in vitro [4].

2. Drug Pharmacology:

2.1 Mechanism of Action

These metal cofactors are essential for multiple biological functions in human lice, including the activity of key metalloproteinases. Since metalloproteinases play a crucial role in egg development, hatching, and overall survival of head lice, their inhibition by abametapir results in lethality [1].

2.2 Pharmacokinetics

Topically applied abametapir is absorbed quickly, with a median Tmax ranging from 0.57 to 1.54 hours in both adults and children. In adults, the average terminal half-life is approximately 21 hours. Systemic exposure tends to be higher with longer application durations, in younger individuals, and in those with lower body mass index. Both the parent compound and its metabolite exhibit strong plasma protein binding. Average elimination half-life of about 71 hours. In vitro findings indicate that the prolonged plasma presence of abametapir carboxyl may inhibit the activity of CYP1A2, CYP2B6, and CYP3A4 enzymes [1].

2.3 Ovicidal Efficacy of Abametapir

Body louse eggs of varying ages were tested for their susceptibility to a prototype formulation. As seen previously with head louse eggs, younger eggs were found to be more vulnerable to treatment than older ones. In the vehicle-treated control groups, about 86% of eggs successfully hatched, with hatching rates remaining consistent across all age groups [4].
Abametapir, a heavy metal–chelating agent, acts by inhibiting metalloproteinases that are essential throughout the louse life cycle. Initial analyses of eggshell washings from newly hatched louse eggs highlighted the key role of metalloproteinases in the hatching process, with their inhibition resulting in complete (100%) prevention of egg hatching. Studies in Drosophila melanogaster further demonstrated that abametapir disrupted ova development at multiple embryonic stages, underscoring the importance of metalloproteinases in both embryogenesis and hatching. The effect of reintroducing specific cations varied between ova and larvae, suggesting that abametapir targets different cations—and consequently, distinct metalloproteinases—vital for the various developmental stages. Treatment with abametapir at 0.74% (w/w) produced complete mortality across all louse egg stages (0–2 days, 3–5 days, and 6–8 days old), with newly laid eggs showing the highest sensitivity [1].

2.4 Transmission

Lice are most often transmitted through direct head-to-head contact, with spread commonly occurring within households. Transmission has also been reported via shared items such as combs, hairbrushes, or hats. They are incapable of jumping or flying, and pets do not serve as vectors [5].

2.5 Diagnosis

Head lice infestation is often misdiagnosed. The presence of nits alone does not confirm active infestation, as they can remain attached to hair shafts for months after successful treatment. Although visual inspection of the scalp and hair is commonly used, it may fail to detect up to three-quarters of cases that can be identified through combing with a fine-toothed detection (“nit”) comb. In one study, this method was also found to be twice as fast as visual inspection in detecting live lice. Combing wet hair has been recommended as well and may offer greater sensitivity compared to combing dry hair [5].

3. Materials and Methods:

3.1 Study Oversight

As part of the clinical development program for Abametapir, two identical phase 3 trials (Study 1 and Study 2) were carried out across multiple sites in the United States. Both studies adhered to the principles of the Declaration of Helsinki, the International Conference on Harmonisation guidelines for Good Clinical Practice, and the requirements of the institutional review boards at each site. The trials were registered at ClinicalTrials.gov under identifiers NCT02060903 and NCT02062060[3].

3.2 Study Subjects

Due to the contagious nature of lice, all household members with infestations were included in the studies. The youngest member of the household with a minimum of three live lice was designated as the index subject for inclusion in the primary analysis, whereas other household members [3].
Exclusion criteria included use of any pediculicide treatment within 14 days prior to study entry or an investigational drug within the previous 30 days. Subjects were also excluded if they presented with visible scalp or skin disorders unrelated to lice infestation (such as eczema or atopic dermatitis) or if they had a history of hypersensitivity to products containing permethrin. In cases where any infested household member was unwilling or ineligible to participate, or if a subject did not reside in the household for the duration of the study, the entire household was excluded from participation [3].

3.3 Study Design

This phase 2 trial was a double-blind, randomized, vehicle-controlled, parallel-group study conducted in participants aged 3 years and older who had an active head lice infestation. The objective was to evaluate the ovicidal activity of a single application of abametapir lotion, compared with vehicle control, applied to the scalp and hair for 10 minutes under supervised conditions at the study site [2].

On day 0 (baseline), index subjects were randomized to receive either abametapir lotion or vehicle lotion, and all non-index household members were given the same treatment as their respective index subject. Each participant was provided with a 200-g bottle of the study medication, along with instructions for home administration by the subject or caregiver on the day it was dispensed. The product was applied as a single treatment to dry hair and scalp, carefully massaged from the hairline at the nape of the neck all the way to the hair tips [3].

Participants were instructed to shield their face and eyes during application. After ensuring complete saturation of the hair and scalp, the product was left in place for 10 minutes before being rinsed out with warm water. Nit combing was prohibited for 14 days prior to and following treatment [3].

3.4 Endpoint

The primary efficacy endpoint was the proportion of index subjects in the intent-to-treat (ITT) population who remained louse-free at all follow-up visits through day 14. Secondary endpoints included the proportion of index subjects who were louse-free at day 1 and day 7. An exploratory endpoint assessed the proportion of all randomized participants (both index and non-index) who achieved louse-free status across all follow-up visits through day 14. Safety assessments comprised monitoring of adverse events as well as evaluations for potential skin, scalp, and eye irritation [3].

3.5 Statistical Analysis

The primary efficacy analysis compared the proportion of hatched eggs before and after treatment between the abametapir lotion group and the vehicle group [2]. The sample size was determined based on the anticipated effect size drawn from a previous phase 2b study. A two-sided, continuity-corrected chi-square test for equality of proportions at a 5% significance level was used for the calculations. To detect a minimum 35% difference in outcomes between the treatment and vehicle groups with 90% statistical power, 48 index subjects per group were needed. Accounting for a potential 10% dropout rate, the enrollment target was set at 53 index subjects (families) per group to ensure at least 48 evaluable participants for the primary endpoint.

The primary and secondary efficacy endpoints in both studies were analyzed using the Cochran–Mantel–Haenszel test, stratified by study site, with significance set at the 5% level. To assess any interaction between treatment group and study site, the Breslow–Day test was employed. If this interaction proved statistically significant ($p < 0.10$), a logistic regression sensitivity analysis was performed to verify the presence of a treatment-by side effect [3].

4.Results of Evaluation of Clinical Studies

4.1:Compliance

The primary efficacy analysis showed that a significantly greater percentage of index subjects achieved treatment success—defined as the absence of live lice at all post-baseline visits—when treated with abametapir lotion compared to the vehicle. In Study 1, the success rates were 81.1% for the abametapir group versus 50.9% for the vehicle group (odds ratio [OR] = 4.01; 95% confidence interval [CI]: 1.70–9.48; P = 0.001). In Study 2, success was observed in 81.8% of abametapir-treated subjects compared to 47.2% in the vehicle group (OR = 5.50; 95% CI: 2.20–13.73; P < 0.001) [3].

4.2:Efficacy

The results confirmed the superior efficacy of abametapir lotion over vehicle, with significantly more index subjects remaining free of live lice through all follow-up visits. In Study 1, 81.1% of participants treated with abametapir were louse-free, compared to 50.9% in the vehicle group (OR = 4.01; 95% CI: 1.70–9.48; P = 0.001). Similarly, in Study 2, 81.8% of abametapir-treated subjects were louse-free versus 47.2% in the vehicle group (OR = 5.50; 95% CI: 2.20–13.73; P < 0.001) [3].

For the secondary endpoints assessed on days 1 and 7, 92.5% of participants in the abametapir group of Study 1 and 87.3% in Study 2 were free of lice by day 1. These rates remained high on day 7—90.6% and 85.5%, respectively. In contrast, the vehicle group showed some initial effect (61.8% in Study 1 and 67.9% in Study 2 on day 1), but these rates declined further by day 7.

An exploratory analysis looked at all randomized subjects (index and non-index) who remained louse-free through day 14. In Study 1, 88.2% of participants in the abametapir group met this criterion compared to 62.0% in the vehicle group (OR = 4.48; 95% CI: 2.65–7.60; P < 0.001). In Study 2, the success rates were 81.0% for abametapir versus 60.5% for the vehicle group (OR = 2.87; 95% CI: 1.72–4.78; P < 0.001) [3].

4.3:Safety

Across both studies, the most common treatment-emergent adverse events included erythema, rash, and a burning sensation on the skin. Hair discoloration was reported in three participants at one site, but this resolved by day 7 and was not considered related to the study drug. No serious adverse events were reported in Study 2. Laboratory assessments—including hematology and biochemistry—revealed no significant or clinically relevant abnormalities after treatment with either abametapir or the vehicle. Overall, abametapir lotion demonstrated a favorable safety profile and was well tolerated [3].

5.Discussion

Abametapir 0.74% lotion (Xeglyze) represents a significant advancement in head lice management through its unique ovicidal mechanism, targeting eggs, nymphs, and adults alike. Unlike older neurotoxic agents such as permethrin or malathion, which often require repeat applications and face rising resistance, abametapir delivers high efficacy with a single 10-minute treatment.

Phase III trials demonstrated >80% treatment success versus 47–51% with vehicle, with rapid louse clearance evident from day 1. Laboratory studies confirm complete egg mortality, removing the need for repeated dosing or nit-combing. The treatment showed a favorable safety profile, with only mild, transient side effects and no systemic toxicity, though further evaluation of CYP450 inhibition and systemic absorption in young children is needed.
Key limitations include the absence of active comparators, restriction of nit-combing, and limited 14-day follow-up. Nevertheless, abametapir's ease of use, single-dose regimen, and novel resistance-avoiding action position it as a strong first-line option. Future studies should clarify long-term outcomes, resistance patterns, pharmacogenomic influences, and cost-effectiveness.

6.Conclusion:

Abametapir 0.74% (Xeglyze) is a safe, single-application treatment that effectively targets all stages of head lice, including eggs. With demonstrated ovicidal activity, strong clinical efficacy, and ease of use, it offers a valuable alternative to traditional pediculicides, supporting better treatment outcomes and adherence in pediculosis capitis management.

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