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Review on Drug Abametapir for the Treatment of Head Lice

Mayuri Gopinath Divekar, Avanti Sahebrao Kale, Afsana Husen Shaikh, Apeksha Somnath Yewale, Ms. Walunj K. B.
Samarth Institute of Pharmacy, Belhe, Maharashtra, India

Abstract: *Pediculushumanuscapitis or head louse, a blood-sucking, wingless arthropod, has been a source of repulsion and embarrassment causing social distress, parental anxiety, and absenteeism. The battle to eradicate this infestation has not been rewarding as the obligate parasite continues to produce resistance to effective first-line pediculicides such as permethrin. Abametapir is a new pediculicide that inhibits the metalloproteinases critical to the hatching process of the eggs. Being ovicidaldrug,it needs a single application. In two large phase 3 studies with 704 subjects aged 26 months, abametapir lotion eliminated lice in 280% of subjects after a single 10-minskin burning. The Food and Drug Administration approved abametapir lotion, 0.74%, for a one-time topical treatment of head louse infestation for patients aged 6 months and older in July 2020. Good efficacy, safety, and a novel mechanism of action make it a welcome addition to the list of effective lousicidal drugs.*

Keywords: pediculicide; Pediculushumanuscapilice Xeglyze; head lice infestation

I. INTRODUCTION

Abametapir is aa metalloproteinase (MMP) inhibitor which is able to target metalloproteinases critical to egg hatching and louse development. Abametapir can inhibit hatching of both head and body louse. Abametapir is capable of chelating heavy metal ions, including iron, copper, and zinc, and is therefore able to interact with a range of targets within the insect that require metal co-factors for function, including metalloproteinases.The head louse (Pediculushumanuscapitis), a blood-sucking arthropod of the suborder Anoplura,
measures about the size of the sesame seed and can crawl with a speed up to 23 cm/min.
Each female lays 8-10 eggs daily at the skin-hair junction and up to 300 eggs during her lifetime. Egg cases, called nits, shaped like oval capsules and glued to hair by an adhesive produced by the mother's accessory gland, are laid preferentially at the temples, behind the ears, and at the back of the neck. 7-10 days later, hatching results in three nymphal stages that moult on the third, fifth, and tenth days.
The length of infestation can be assessed by measuring the farthest distance of eggs from the scalp and comparing it to the growth rate of hair; a distance of >1/4 in may indicate an inactive, old infestation.Prevalence of head louse infestation is estimated to range between 0.7% and 59% in Asian population.Head-to-head contact can transmit the infestation to caregivers and close contacts.
Abametapir chelates heavy metal cations and inhibits metalloproteinases critical to louse ova development, hatching, and adult survival. In phase II, abametapir had direct ovicidal activity inhibiting 100% of treated louse eggs from hatching, compared with 64% in the vehicle-treated group. In two identical phase III clinical trials, subjects treated with a single 10-minute application of abametapir had greater treatment success compared with vehicle-treated subjects, with 81.1% success versus 50.9% in study 1 ($P = 0.001$) and 81.8% versus 47.2% in study 2 ($P < 0.001$). Abametapir was well tolerated, with only mild adverse effects.

Abametapir

Abametapir, sold under the brand name Xeglyze, is a medication used for the treatment of head lice infestation in people six months of age and older.Abametapir is a metalloproteinase inhibitor.Abametapir was approved for medical use in the United States in July 2020.The U.S. Food and Drug Administration (FDA) considers it to be a first-in-class medication.The U.S. Food and Drug Administration (FDA) approved abametapir based on evidence from two identical

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clinical trials of 699 participants with head lice.The trials were conducted at fourteen sites in the United States.The benefit and side effects of abametapir were evaluated in two clinical trials that enrolled participants with head lice who were at least six months old. About half of all enrolled participants was randomly assigned to abametapir and the other half to placebo. Abametapir lotion or placebo lotion were applied once as a ten-minute treatment to infested hair.The benefit of abametapir in comparison to placebo was assessed after 1, 7 and 14 days by comparing the counts of participants in each group who were free of live lice.Abametapir carboxyl has a plasma protein binding of 96.0–97.5% and is the predominant of the three substances in the circulation, having a Cmax 30 times and an area under the curve (AUC) 250 times that of abametapir itself.

Pharmacodynamics:-

Abametapir has been shown to inhibit all stages of embryo development in both head and body lice1 by interfering with enzymes critical to this process. It is relatively unique amongst lice treatments in that it requires only a single application, whereas many current therapies require two applications, due to its exceptional potency and unique mechanism.1,4 Its predominant metabolite, abametapir carboxyl, has a prolonged residence time in the body, with an estimated half-life of 71 ± 40 hours or longer in adults - as this metabolite has been shown to inhibit cytochrome P450 enzymes in vitro, the use of substrates of CYP3A4, CYP2B6, or CYP1A2 should be avoided for two weeks following the administration of abametapir.

Mechanism of action

There are several metalloproteinases (enzymes requiring metal co-factors to function)1 involved in the process of louse egg hatching and survival.2,4 In vitro studies have demonstrated that metal-chelating agents can inhibit the activity of these proteins,2 and may therefore be valuable pediculicidal agents. Abametapir is a metalloproteinase inhibitor that targets louse metalloproteinases which are critical to their development and hatching.

Half life:-

The elimination half-lives of abametapir and its metabolites have not been well-characterized, but the estimated half-life of abametapir carboxyl is 71 ± 40 hours (or longer) in adults.

Data synthesis:

Abametapir chelates heavy metal cations and inhibits metalloproteinases critical to louse ova development, hatching, and adult survival. In phase II, abametapir had direct ovicidal activity inhibiting 100% of treated louse eggs from hatching, compared with 64% in the vehicle-treated group. In two identical phase III clinical trials, subjects treated with a single 10-minute application of abametapir had greater treatment success compared with vehicle-treated subjects, with 81.1% success versus 50.9% in study 1 ($P = 0.001$) and 81.8% versus 47.2% in study 2 ($P < 0.001$). Abametapir was well tolerated, with only mild adverse effects.

Abametapir effectiveness

In two randomized, double-blind, controlled studies involving a total of 704 patients older than six months, treatment with abametapir resulted in a greater likelihood of complete clearance of head lice at 14 days (85.9% in the treatment

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group vs. 61.3% in the placebo group; P < .001; number needed to treat = 4). Results were similar in children and adults.Ovicidal activity was demonstrated in a study of 50 patients. Eggs were collected before and after treatment with abametapir or vehicle. Compared with untreated eggs, the reduction in egg hatching was 92.9% for abametapir vs. 42.3% for vehicle (P < .001).2 Abametapir has not been compared with other nonprescription or prescription treatments of head lice, although older treatments may have clearance rates of less than 70% following two applications.

Study Design

This phase 2 study was a double-blind, randomized, vehicle-controlled, parallel-group study in subjects aged 3 years and older with an active head lice infestation. The study was designed to assess the ovicidal efficacy of a single application of abametapir lotion compared with a vehicle control, when applied to the scalp and hair for 10 minutes at the study site. Fifty subjects were randomized 1:1 to receive either abametapir lotion or vehicle lotion.

All subjects completed a screening visit (days −7 to 0) in which trained evaluators systematically examined the scalps of the subjects for up to 15 minutes to detect any live lice and eggs. Subjects were randomized to either abametapir lotion or vehicle lotion. On day 0, before application of the investigational product, at least 5 undamaged eggs located on hair shafts <1 cm from the scalp were randomly selected as untreated controls and removed from each subject's head by hair clipping. Study drug (abametapir lotion or vehicle lotion) was applied to the dry scalp and hair, left for 10 minutes, and then rinsed with warm water and towel dried. Immediately after treatment, the random egg collection process was repeated. Hair shafts collected at the site both before and after treatment were microscopically examined to assess egg viability; nonviable eggs (non-ellipsoid, squashed, flattened, or crushed) were discarded. Viable eggs were incubated at 30°C (±1°C) and ~60% relative humidity for 14 days. All eggs were then examined by an independent assessor to determine whether eggs were hatched, partially hatched, or unhatched. The assessor was blinded to the treatment assignments and the time of collection of the egg samples. The proportion of pretreatment versus posttreatment hatched eggs was compared across treatment groups following incubation. Subjects returned to the site on day 1 (+1) and day 7 (+2) to assess for the presence of live lice.

Uses

Abametapir is a pediculicide metalloproteinase used topically in the treatment of head lice infection. Abametapir is a novel pediculicidal metalloproteinase inhibitor used to treat infestations of head lice.It is indicated for the topical treatment of head lice infestation in people six months of age and older.

Interaction

Abametapir blocks the liver enzymes CYP3A4, CYP2B6 and CYP1A2 in vitro. A single application of the drug may lead to increased blood concentrations of drugs that are metabolized by these enzymes.

Abametapir side effects

The most common side effects include skin redness, rash, skin burning sensation, skin inflammation, vomiting, eye irritation, skin itching, and hair color changes.

Result

Abametapir lotion, 0.74%, was effective at clearing active head louse infestations through day 14 in subjects aged 6 months and older. All adverse events (including one serious but unrelated to study drug) resolved uneventfully.In the intent-to-treat population (index subjects, N = 216), 81.5% of subjects treated with abametapir lotion were louse free through day 14 after a single treatment, versus 49.1% with vehicle (P < 0.001). The most frequently reported adverse events were erythema (4.0%), rash (3.2%), and skin burning sensation (2.6%).

II. CONCLUSION

Abametapir is a newly Food and Drug Administration (FDA)-approved single-application treatment for head lice in patients aged six months and older. Its direct ovicidal and lousicidal activity is effective in treating head lice

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infestations with a single application. In the face of growing resistance to current pediculicides, Abametapir offers a safe and effective new treatment option for the management of head lice.

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