

Literature Scan: Topical Antiparasitics

Date of Review: March 2016

Date of Last Review: September 2013

Literature Search: August 2013-December 2015

Current Status of PDL Class:

See **Appendix 1**.

Conclusions:

- There is no new clinical evidence that can further inform PDL decisions for topical antiparasitics.

Recommendations:

- No further review or research needed. After evaluation of comparative drugs costs in the executive session, no changes to the Preferred Drug List (PDL) recommended.

Previous Conclusions:

- There is no new clinical evidence for efficacy or safety that disputes permethrin as first-line therapy for the treatment of lice.
- No further research or review needed at this time.

Previous Recommendations:

- Evaluate comparative costs in executive session.

Methods:

A Medline literature search for new systematic reviews and randomized controlled trials (RCTs) assessing clinically relevant outcomes to active controls, or placebo if needed, was conducted. A summary of the clinical trials is available in **Appendix 2** with abstracts presented in **Appendix 3**. The Medline search strategy used for this literature scan is available in **Appendix 4**, which includes dates, search terms and limits used. The OHSU Drug Effectiveness Review Project, Agency for Healthcare Research and Quality (AHRQ), Cochrane Collection, National Institute for Health and Clinical Excellence (NICE), Department of Veterans Affairs, BMJ Clinical Evidence, and the Canadian Agency for Drugs and Technologies in Health (CADTH) resources were manually searched for high quality and relevant systematic reviews. When necessary, systematic reviews are critically appraised for quality using the AMSTAR tool and clinical practice guidelines using the AGREE tool. The FDA website was searched for new drug approvals, indications, and pertinent safety alerts. Finally, the AHRQ National Guideline Clearinghouse (NGC) was searched for updated and recent evidence-based guidelines.

The primary focus of the evidence is on high quality systematic reviews and evidence-based guidelines. Randomized controlled trials will be emphasized if evidence is lacking or insufficient from those preferred sources.

New Systematic Reviews:

A Cochrane review assessed prophylactic interventions of drug and non-drug treatments including topical antiparasitics for preventing the spread of infestation in close contacts of people with scabies, but was unable to provide recommendations based on a lack of well-designed RCTs.¹

New Guidelines:

The American Academy of Pediatrics issued a revised clinical report regarding treatment protocols and provided guidance for the management of children with head lice in the school setting.² Permethrin 1% or pyrethrins were considered as reasonable first choices for primary treatment of active infestations unless evidence of community resistance proven.² Benzyl alcohol 5% was a suggested option for children older than 6 months. Use of malathion 0.5% lotion was not recommended in children younger than 6 years due to unestablished safety and effectiveness, however, the authors noted that the agent could be used for children 2 years or older in areas with known resistance to permethrin or pyrethrins or for a patient with a failed response to permethrin or pyrethrins.² Authors identified the newer agents spinosad and topical ivermectin as potential options for treatment-resistant cases but noted limitations due to high cost.² Specific comparative efficacy and safety between the available agents were not elucidated in the guidance document.

2013 guidelines for the diagnosis and treatment of pediculosis capitis in children and adults were released by the University of Texas, School of Nursing, Family Nurse Practitioner Program.³ Methods used to assess the strength of the evidence included expert consensus and a rating scheme based on the U.S. Preventive Services Task Force [USPSTF] criteria of high, moderate, or low quality. The scheme for grading recommendations was based on the US Preventative Services Task Force Ratings A (substantial benefit), B (moderate benefit), C (minimal benefit), D (no net benefit/harm), and I (inconclusive benefit).

Recommended topical pharmacologic regimens³:

- Permethrin 1% cream rinse, pyrethrin 0.33%, and piperonyl butoxide 4% all have well established safety profiles and are recommended as first line treatment of patients 2 months and older unless regional resistance is documented (Evidence Moderate, Recommendation B).
- 0.5% malathion lotion has a favorable safety profile and is effective with low observed resistance; use is contraindicated in neonates and infants (Evidence Moderate, Recommendation B).
- Ivermectin 0.5% topical lotion was FDA approved in February 2012 for treatment of head lice in patients greater than 6 months of age (Evidence Moderate, Recommendation B)
- Spinosad 0.9% topical suspension was FDA approved in January 2011 for patients 4 years and older for effective and convenient treatment for head lice (Evidence Low, Recommendation B).
- Benzyl alcohol 5% lotion is the first U.S. Food and Drug Administration (FDA)-approved, non-neurotoxic prescription product for treating head lice that is shown to be safe and effective in patients 6 months and older (Evidence Low, Recommendation B).

Alternative topical pharmacologic regimens³:

- Lindane 1% shampoo should be reserved for patients for whom other lice treatments have failed and/or for persons who cannot tolerate other pediculicides; use in infants and children is cautioned (Evidence Moderate, Recommendation C).

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- Essential oils: There are no formal controlled clinical trials demonstrating efficacy, potential side effects or toxicity of eucalyptus, lavender and tea tree oil, and therefore, they cannot be recommended as a treatment option (Evidence Low, Recommendation I).

New FDA Drug Approvals:

None identified.

New Formulations/Indications:

The FDA modified the spinosad 0.9% suspension indication to include patients 6 months of age and older with head lice infestation.⁴

New FDA Safety Alerts:

None identified.

References:

1. FitzGerald D, Grainger RJ, and Reid A. Interventions for Preventing the Spread of Infestation in Close Contacts of People with Scabies. *Cochrane Database of Syst Rev*. 2014 Feb 24;2:CD009943. doi:10.1002/14651858.CD009943.pub2.
2. Devore CD, Schutze GE, and the Council on School Health and Committee on Infectious Diseases. Head Lice. *Pediatrics*. 2015; 135(5): e1355–65. doi:10.1542/peds.2015-0746.
3. Guidelines for the diagnosis and Treatment of Pediculosis Capitis (head Lice) in Children and Adults 2013. National Guideline Clearinghouse (NGC). Available at <https://www.guideline.gov/content.aspx?id=46429>. Accessed December 14, 2015.
4. Natroba (spinosad topical suspension, 0.9%) [Prescribing Information]. Carmel, IN: ParaPRO LLC, December 2014.

Appendix 1: Current Status on Preferred Drug List

ROUTE	FORMULATION	BRAND	GENERIC	PDL
TOPICAL	SHAMPOO	LICE KILLING	PIPERONYL BUTOXIDE/PYRETHRINS	Y
TOPICAL	SHAMPOO	LICE TREATMENT	PIPERONYL BUTOXIDE/PYRETHRINS	Y
TOPICAL	LIQUID	PYRETHRIN LICE TREATMENT	PIPERONYL BUTOXIDE/PYRETHRINS	Y
TOPICAL	LIQUID	LICE TREATMENT	PERMETHRIN	Y
TOPICAL	CREAM (G)	ELIMITE	PERMETHRIN	Y
TOPICAL	CREAM (G)	PERMETHRIN	PERMETHRIN	Y
TOPICAL	KIT	LICE SOLUTION	PIP BUTOX/PYRETHRINS/PERMETH	Y
TOPICAL	LOTION	LINDANE	LINDANE	N
TOPICAL	SHAMPOO	LINDANE	LINDANE	N
TOPICAL	CREAM (G)	EURAX	CROTAMITON	N
TOPICAL	LOTION	EURAX	CROTAMITON	N
TOPICAL	LOTION	MALATHION	MALATHION	N
TOPICAL	LOTION	OVIDE	MALATHION	N
TOPICAL	LOTION	ULESFIA	BENZYL ALCOHOL	N
TOPICAL	LOTION	SKLICE	IVERMECTIN	N
TOPICAL	SUSPENSION	NATROBA	SPINOSAD	N
TOPICAL	SUSPENSION	SPINOSAD	SPINOSAD	N

Appendix 2: New Clinical Trials

A total of 22 citations were manually reviewed from the literature search. After further review, 21 trials were excluded because of wrong study design, comparator, or outcome studied. The remaining trial is briefly described in the table below. The full abstract is included in Appendix 3.

Table: Description of Clinical Trials

Study	Comparison	Population	Primary Outcome	Results
Goldust et al., 2014, Iran	Topical ivermectin (TI) versus crotamiton cream 10% (CC)	340 subjects (190 male, 150 female, ages 4-72). TI (n = 170) and CC (n = 170)	Cure of scabies over 4-week period. Cure = absence of new lesions and healing of old Reinfestation = cure at 2 weeks but new lesion development at end of 4 weeks Treatment failure = confirmed new lesions at 2-week follow-up	No significant difference between cure rate of ivermectin vs. crotamiton cream 10% at 2 weeks: 64.7% vs. 41.2% respectively (P = 0.72). Ivermectin cure rate was superior to crotamiton cream 10% at 4 weeks: 82.3% vs. 64.7% respectively (P = 0.043). Allocation procedure not disclosed Unexplained losses after first follow-up prior to initial enrollment <u>Adverse effects</u> Irritation: 18% (TI) vs 12% (CC)

Appendix 3: Abstract of Clinical Trial

Topical ivermectin versus crotamiton cream 10% for the treatment of scabies. Goldust M; Rezaee E; Raghiafar R. International Journal of Dermatology. 53(7):904-8, 2014 Jul. UI: 24898622

Scabies, known colloquially as the 7-year itch, is a contagious skin infection that occurs among humans and other animals. The treatment of choice is still controversial. The aim of this study was to compare the efficacy and safety of topical ivermectin vs. crotamiton cream 10% for the treatment of scabies. In total, 340 patients with scabies were enrolled, and randomized into two groups. The first group received 1% ivermectin applied topically to the affected skin. The dose employed was 400 mug/kg, repeated once the following week, and the second group received crotamiton 10% cream and were told to apply this twice daily for five consecutive days. Treatment was evaluated at intervals of two and four weeks, and if there was treatment failure at the 2-week follow-up, treatment was repeated. Two applications of topical ivermectin provided a cure rate of 64.7% at the 2-week follow-up, which increased to 82.3% at the 4-week follow-up after repeating the treatment. Treatment with single applications of crotamiton cream 10% was effective in 41.2% of patients at the 2-week follow-up, which increased to 64.7% at the 4-week follow-up after this treatment was repeated. Ivermectin was quite safe in our cases. Two applications of ivermectin were as effective as single applications of crotamiton 10% cream at the 2-week follow-up. After repeating the treatment, ivermectin was superior to crotamiton cream 10% at the 4-week follow-up.

Appendix 4: Medline Search Strategy

Ovid MEDLINE(R) without Revisions 1996 to November Week 3 2015

1 benzyl alcohol.mp. or exp Benzyl Alcohol/1235

2 ivermectin.mp. or exp Ivermectin/4296

3 lindane.mp. or exp Lindane/2105

4 malathion.mp. or exp Malathion/ 1579

5 permethrin.mp. or exp Permethrin/2119

6 piperonyl butoxide.mp. or exp Piperonyl Butoxide/614

7 pyrethrin.mp. or exp Pyrethrins/5381

8 spinosad.mp./517

9 crotamiton.mp./65

10 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9/ 15067

11 exp Administration, Topical/ or topical.mp.78881

12 10 and 11/ 936

13 limit 12 to (English language and humans and yr="2013 -Current"

and (clinical trial, all or clinical trial or comparative study or controlled clinical trial

or guideline or meta analysis or practice guideline or pragmatic clinical trial or

randomized controlled trial or systematic reviews))/22