

Antiparasitic Agents, Topical Review

11/18/2010

Copyright © 2008 - 2010 by Provider Synergies, L.L.C. All rights reserved.
Printed in the United States of America.

All rights reserved. No part of this publication may be reproduced or transmitted in any form or by any means, electronic or mechanical, including photocopying, recording, digital scanning, or via any information storage and retrieval system without the express written consent of Provider Synergies, L.L.C.

All requests for permission should be mailed to:

*Attention: Copyright Administrator
Intellectual Property Department
Provider Synergies, L.L.C.
10101 Alliance Rd. Ste 201
Cincinnati, Ohio 45242*

The materials contained herein represent the opinions of the collective authors and editors and should not be construed to be the official representation of any professional organization or group, any state Pharmacy and Therapeutics committee, any state Medicaid Agency, or any other clinical committee. This material is not intended to be relied upon as medical advice for specific medical cases and nothing contained herein should be relied upon by any patient, medical professional or layperson seeking information about a specific course of treatment for a specific medical condition. All readers of this material are responsible for independently obtaining medical advice and guidance from their own physician and/or other medical professional in regard to the best course of treatment for their specific medical condition. This publication, inclusive of all forms contained herein, is intended to be educational in nature and is intended to be used for informational purposes only. Send comments and suggestions to PSTCReDitor@magellanhealth.com.



Together, we can do more.

Antiparasitic Agents, Topical Review

FDA-Approved Indications

Drug	Manufacturer	FDA-Approved Indications
Prescription		
benzyl alcohol (Ulesfia™) ¹	Shionogi Pharma	Treatment of head lice
crotamiton (Eurax®) ²	Westwood-Squibb	Treatment of scabies Symptomatic treatment of pruritis
lindane ³	generic	Treatment of head lice and ova Treatment of crab lice and ova Treatment of scabies
malathion (Ovide®) ⁴	generic	Treatment of head lice and ova
permethrin 5% cream (Acticin®, Elimite®) ⁵	generic	Treatment of scabies
Over-The-Counter (OTC)		
permethrin 1% lotion (Nix®) ⁶	generic	Treatment of head lice Prophylaxis during head lice epidemic
pyrethrins/piperonyl butoxide (A-200®, Pronto®, RID®) ⁷	generic	Treatment of head lice Treatment of body lice Treatment of crab lice

Lindane is reserved for patients who cannot tolerate other approved therapies or have failed treatment with other approved therapies.

Overview

Head lice, or *Pediculus humanus capitis*, are a worldwide public health concern affecting persons of all ages and socioeconomic backgrounds. In the U.S., it is most common among children three to 12 years old and accounts for six to 12 million annual infestations.⁸ Head lice infestations are not typically associated with morbidity, are not a sign of uncleanliness, and do not transmit systemic disease, although secondary methicillin-resistant *Staphylococcus aureus* (MRSA) or streptococcal infections may occur.^{9,10,11} Pediculosis is a source of social stigma and embarrassment and can prevent children with nits from attending school where a “no nit” policy is in place.¹² Itching is the primary symptom of pediculosis which results from an allergic reaction to the saliva lice inject during feeding.

The primary mode of head lice transmission is direct head-to-head contact. Lice crawl using adapted claws; they do not jump, hop, or fly. Once off the host, head lice only survive 15 to 20 hours.¹³ In the U.S., head lice affects all socioeconomic groups; there is less infestation among

African-Americans than other races, possibly due to a lack of adaptation of the lice claws to grasp specific shape and width hair shafts; hair length is not a factor.¹⁴

Topical pediculicides, toxic to the louse central nervous system (CNS), are the initial treatment choice for treatment of head lice.¹⁵ The 2010 American Academy of Pediatrics (AAP) Head Lice Guidelines recommend topical OTC permethrin 1% or pyrethrins as first-line for head lice when resistance to these products is not suspected.¹⁶ When resistance to these agents is confirmed or treatment fails, malathion (Ovide) can be used in children two years and older or benzyl alcohol (Ulesfia) can be used in children older than six months. Lindane is no longer recommended by the AAP due to concerns with neurotoxicity, rare severe seizures in children, low ovicidal activity, and worldwide reports of resistance.

The 2010 AAP guidelines recommend checking all household members for head lice. Those with live lice or nits within 1 cm of the scalp should be treated.¹⁷ The AAP also considers it prudent to prophylactically treat bedmates even if no live lice are found. The AAP does not recommend the routine use of pediculicide sprays since the nits are unlikely to incubate and hatch at room temperature or survive off the scalp beyond 48 hours. Clothing, furniture, or carpeting that has come in contact with the infested person 24 to 48 hours prior to treatment may be washed.

For treatment for *Pediculosis pubis*, or crab lice, the 2006 Centers for Disease Control and Prevention (CDC) Sexually Transmitted Diseases Treatment Guidelines recommend permethrin 1% cream or pyrethrins with piperonyl butoxide (RID[®]) as first-line despite growing resistance.¹⁸ Malathion or oral ivermectin (Stromectol[®]) are considered alternative regimens. Lindane is second-line. All sexual contacts should be treated at the same time to prevent cross reinfection.

Causes of treatment failure in pediculosis or scabies include misdiagnosis, noncompliance, reinfestation, resistance, inadequate treatment, and lack of drug ovicidal or residual killing properties. Incorrect pediculicide application should be considered first when there is treatment failure. No currently available pediculicide is 100 percent ovicidal; resistance to permethrin, lindane, pyrethrins, and the United Kingdom formulation of malathion has been reported.^{19,20,21,22,23,24,25,26} However, the actual rates of resistance to specific products can vary by region and are not known. Benzyl alcohol (Ulesfia) resistance is unlikely.²⁷ Resistance should be suspected after the second treatment if live lice are still present two to three days after a product has been applied correctly, and no other cause of failure can be identified. Subsequent treatment should be with a different class.^{28,29} Using higher strengths of permethrin are not more efficacious.^{30,31}

Scabies is a major public health concern in many poor regions. Scabies is caused by an eight-legged obligate human parasitic mite *Sarcoptes scabiei* and results in intense pruritis which is due to a delayed type-IV hypersensitivity reaction to the mite, its feces, and eggs. There is also a characteristic rash and distribution pattern. It can affect the entire body, but in adults, the head and neck are usually not affected. The female mite burrows under the skin and lays 10 to 25 eggs before dying. The eggs hatch in three days, leave the burrow for the skin surface, and mature into adults. Scabies can cause morbidity from secondary infections. If left untreated, staphylococcal infections including impetigo, ecthyma, paronychia, and furunculosis can occur.^{32,33} Transmission of scabies is usually from direct person-to-person contact. The mites can survive off a host for 24 to 36 hours and longer in colder temperatures.^{34,35} Crusted scabies or Norwegian scabies, an aggressive form of scabies, can occur in immunocompromised patients.

The 2006 CDC Sexually Transmitted Diseases (STD) Treatment Guidelines recommends topical permethrin 5% or oral ivermectin as first-line for the treatment of scabies, despite

resistance to permethrin.³⁶ Lindane is second-line due to associated CNS toxicity and resistance. Crotamiton (Eurax) is not mentioned in the CDC guidelines; however, it does have a role as an antipruritic in scabies. All family members and close contacts must be prophylactically treated at the same time. Unlike head lice, environmental measures are essential for successful treatment of scabies, since mites can survive off the host. Clothes, linens, and towels must be washed with hot water and heat dried, dry-cleaned, or placed in a sealed plastic bag for at least 72 hours.

Systemic agents are used in the treatment head lice, crab lice, and scabies, particularly in resistant cases. This review focuses on the available prescription topical antiparasitic treatments for head lice, crab lice, and scabies.

Pharmacology^{37,38,39,40,41,42}

The exact mechanism of crotamiton (Eurax) is not known. It has scabicial activity against *Propionibacterium acnes* and *S. scabiei*, as well as antipruritic actions.

Benzyl alcohol (Ulesfia) is a topical pediculicide. It inhibits lice from closing their respiratory spiracles, which results in obstruction of the spiracles by the vehicle and subsequent asphyxiation of the lice. Benzyl alcohol does not have ovicidal activity; therefore, therapy must be repeated after seven days.

Lindane is directly absorbed by parasites and their ova. It non-competitively inhibits gamma amino butyric acid (GABA) receptors. Lindane stimulates the nervous system, resulting in seizures and death of the parasites. Lindane resistance is thought to be via the GABA receptor becoming less sensitive to GABA antagonists.

Malathion (Ovide) is an organophosphate which acts as a pediculicide by inhibiting cholinesterase activity *in vivo*. Malathion resistance is thought to occur by increased levels of carboxylesterases that are involved in the drugs metabolism into non-malaxon intermediates.

Permethrin (Acticin, Elimite) is a synthetic pyrethroid which inhibits sodium ion influx through nerve cell membrane channels in ectoparasites, resulting in delayed repolarization and resultant paralysis and death of the parasites. Pyrethroid resistance is mediated by mutation of the alpha subunit gene of the neuronal voltage-gated sodium channel, conferring decreased sensitivity of the channel to pyrethroids. This is referred to as knock-down resistance.

None of the pediculicides are 100 percent ovicidal. Malathion and permethrin have high ovicidal activity.

Pharmacokinetics^{43,44,45,46,47}

Benzyl alcohol (Ulesfia) has shown systemic concentrations ranging from 1.97 to 2.99 mcg/mL 30 minutes post treatment and 1.63 mcg/mL one hour after treatment.

The degree of systemic absorption following topical administration of crotamiton (Eurax) or malathion (Ovide) has not been determined, although the potential exists.

Lindane lotion and shampoo have shown a systemic absorption of up to 10 percent. Lindane is rapidly distributed followed by a longer beta-elimination phase. It is metabolized hepatically, excreted in the urine and feces, and has four major primary and two major secondary

metabolites. Its half-life is about 18 hours.

Permethrin has a systemic absorption of two percent or less. It is metabolized by ester hydrolysis in the liver to inactive metabolites and is excreted primarily in the urine.

Contraindications/Warnings^{48,49,50,51,52}

Lindane is contraindicated in uncontrolled seizure disorders, crusted (Norwegian) scabies, or any condition which may increase systemic absorption. It is also contraindicated in premature infants. Lindane carries a boxed warning as its use may be associated with severe neurologic toxicities. Caution should be exercised in patients weighing less than 50 kg, particularly in infants, children, elderly, or patients with history of seizures, conditions which may increase risk of seizures, or taking medications which may lower the seizure threshold.

Malathion (Ovide) is contraindicated in neonates and infants. Benzyl alcohol (Ulesfia) should not be used in patients less than six months old. Neonates (less than one month old or preterm infants with a corrected age of less than 44 weeks) can be at risk for gasping syndrome if treated with benzyl alcohol lotion. Intravenous (IV) administration of products containing benzyl alcohol has been associated with neonatal gasping syndrome consisting of severe metabolic acidosis, gasping respirations, progressive hypotension, seizures, CNS depression, intraventricular hemorrhage, and death in preterm, low birth weight infants. Permethrin (Acticin, Elimite) is contraindicated in infants less than two months old. Treatment with permethrin may temporarily exacerbate symptoms of itching, redness, and swelling. Itching may occur even after successful killing of lice. Rare cases of asthma exacerbations have been reported with use of pyrethroid-based products such as permethrin in patients with ragweed or chrysanthemum allergies.⁵³

These agents are for external use only. Contact with face, eyes, and mucous membranes should be avoided. Acutely inflamed or raw skin should also not come into contact with these products.

Avoid fire, flame, smoking, and electric heat sources for hair (e.g., hair dryers) following use of malathion; it contains 78 percent isopropyl alcohol and is highly flammable.

Drug Interactions^{54,55,56,57,58}

No drug interactions have been reported for crotamiton (Eurax), malathion (Ovide), or permethrin (Acticin, Elimite). Increased toxicity has been reported with the use of lindane and drugs which can lower seizure threshold. Oils, creams, or ointments may enhance lindane absorption; concomitant use should be avoided. Drug interaction studies were not conducted for benzyl alcohol (Ulesfia).

Adverse Effects^{59,60,61,62,63}

Drug	Dermatitis	Pruritis/ Rash	Burning/ Stinging	Paresthesia	Erythema	Headache	Seizures
benzyl alcohol (Ulesfia)*	<1	12 (pruritis) <1 (rash)	<1	<1	10	nr	nr**
crotamiton (Eurax)	reported	reported	nr	nr	nr	nr	nr
lindane	reported	reported	nr	reported	nr	reported	reported
Malathion (Ovide)	reported	nr	nr	nr	nr	nr	nr
permethrin (Acticin, Elimite)	nr	7 (pruritis) ≤ 2 (rash)	10	≤ 2	≤ 2	reported	nr

Adverse effects data are reported as percentages. Adverse effects data are obtained from package inserts and are not meant to be comparative or all inclusive. nr = not reported

* Pyoderma and ocular irritation were reported in seven and six percent of patients taking benzyl alcohol, respectively.

** IV products containing benzyl alcohol have been associated with neonatal gasping syndrome characterized by a number of symptoms including seizures.

Special Populations^{64,65,66,67,68}

Pediatrics

Safety and effectiveness of benzyl alcohol (Ulesfia) have not been established in patients less than six months old. Pyrethrin/piperonyl butoxide topicals should not be used in children less than two years old.

Safety and effectiveness of crotamiton (Eurax) have not been established in pediatrics.

Extreme caution should be exercised for lindane in patients who weigh less than 50 kg, particularly in infants and children. Lindane is contraindicated in premature infants.

Safety and effectiveness of malathion (Ovide) have not been established in pediatrics younger than six years old; its use is contraindicated in neonates and infants.

Safety and effectiveness of OTC and prescription permethrin (Acticin, Elimite) have not been established in patients less than two months old.

Pregnancy

Crotamiton and lindane are classified as Pregnancy Category C. Benzyl alcohol, malathion, and permethrin are Pregnancy Category B.

Hepatic Impairment

Lindane must be used with caution in patients with hepatic impairment.

Geriatrics

The safety of benzyl alcohol has not been established in patients over 60 years old.

Dosages

Drug	Instructions	Availability
Prescription		
benzyl alcohol (Ulesfia) ⁶⁹	Lice: Apply to dry hair and scalp. Rinse after 10 minutes. Repeat treatment in seven days.	5% lotion
crotamiton (Eurax) ⁷⁰	Scabies: Apply from neck to toes as directed; repeat in 24 hours. Rinse 48 hours after final application, then repeat treatment in seven to 10 days if live mites are still present. Pruritis: Apply to affected areas as directed; repeat as needed.	10% cream, lotion
lindane ⁷¹	Lice: Apply <u>shampoo</u> once to hair as directed; do not retreat. Scabies: Apply <u>lotion</u> once from neck to toes as directed. Rinse after eight to 12 hours; do not retreat.	1% lotion 1% shampoo
malathion (Ovide) ⁷²	Lice: Apply once to dry hair as directed. Rinse after eight to 12 hours; repeat in seven to nine days if needed.	0.5% lotion
permethrin (Acticin, Elimite) ⁷³	Scabies: Apply once from head to toe. Rinse after eight to 14 hours as directed. Repeat in 14 days if live mites are present.	5% cream
OTC		
permethrin (Nix) ⁷⁴	Lice treatment: Apply to hair and scalp as directed. Rinse after 10 minutes. If live lice are seen seven days or more after the first application, a second treatment should be given. Lice prophylaxis: Apply to hair and scalp as directed. Rinse after 10 minutes. In epidemic settings, a second prophylactic application is recommended two weeks after the first application.	1% lotion
pyrethrins/piperonyl butoxide (A-200, Pronto, RID) ⁷⁵	Lice: Apply to dry hair and scalp or skin as directed. Rinse after 10 minutes. Repeat application once in seven to 10 days.	0.33%/4% shampoo, topical foam

Previous recommendations have instructed patients to re-treat in seven to 10 days; however, new evidence based on the life cycle of lice suggests that re-treatment at day nine is optimal. An alternate schedule of three treatments with non-ovicidal products on days zero, seven, and 13 to 15 has been proposed.

Before application of crotamiton, the affected skin should be thoroughly washed and loose scales scrubbed, rinsed, and towel dried.

Lindane shampoo should be applied to dry hair and massaged for four minutes; water is added gradually to create lather. Most patients will require one ounce of shampoo. Some patients may require two ounces of shampoo based on length and density of hair.

Most patients with scabies will require one ounce of permethrin 5% cream.

These agents require application to the head, base of the neck, and behind the ears.

Clinical Trials

Search Strategy

Articles were identified through searches performed on PubMed and review of information sent by manufacturers. Search strategy included the FDA-approved use of all drugs in this class, pediculosis capitis, pediculosis pubis, and scabies. Randomized controlled comparative trials for FDA-approved indications are considered the most relevant in this category. Studies included for analysis in the review were published in English, performed with human participants and randomly allocated participants to comparison groups. In addition, studies must contain clearly stated, predetermined outcome measure(s) of known or probable clinical importance, use data analysis techniques consistent with the study question, and include follow-up (endpoint assessment) of at least 80 percent of participants entering the investigation. Despite some inherent bias found in all studies including those sponsored and/or funded by pharmaceutical manufacturers, the studies in this therapeutic class review were determined to have results or conclusions that do not suggest systematic error in their experimental study design. While the potential influence of manufacturer sponsorship/funding must be considered, the studies in this review have also been evaluated for validity and importance.

There are few well-designed studies for head lice; a number of the studies compare the topical agents to agents outside of this review, so they were not included. There are also few well-designed studies for scabies. A number of the studies compare the topical agents to oral therapy, so they were not included. There were no acceptable studies found for crab lice. Due to the lack of acceptable data, this evaluation includes studies performed versus permethrin 1% OTC (Nix), a lower strength than the prescription product included in this review. Open-label and pooled data were determined to be unacceptable. Many studies use the investigator-blinded design rather than using the double-blinded method and were included. Only placebo-controlled trials are available for benzyl alcohol (Ulesfia) and are included.

Head Lice

malathion (Ovide) and permethrin (Nix)

A randomized, investigator-blinded study of 66 children, mean age of 11.4 years old, with head lice compared malathion 0.5% lotion to permethrin 1% creme rinse.⁷⁶ Both agents were applied according to label instructions, except malathion was applied for a reduced time of 20 minutes instead of the approved label of eight to 12 hours. At day eight, patients still with live lice were retreated with the same agent they were initially treated with on day one. Ovicidal and pediculicidal efficacy were evaluated on days eight and 15. Treatment success was defined as being free of lice and viable eggs at day 15. Malathion was 98 percent pediculicidal and ovicidal versus 55 percent for permethrin at day 15 ($p < 0.0001$). At day eight, 50 percent less malathion patients required treatment versus the permethrin group. The reinfestation rate for malathion versus permethrin was zero percent versus 33 percent, respectively.

malathion gel, malathion (Ovide) and permethrin (Nix)

A randomized, investigator-blinded, parallel-group, active-controlled study of 172 patients with head lice compared malathion 0.5% gel (30-, 60-, 90-minute applications), malathion 0.5% lotion (eight- to 12-hour applications), and permethrin 1% creme rinse.⁷⁷ Patients were treated on day one and re-evaluated on day eight; retreatment was done with the same product as given on day one if live lice were present. Cure was defined as absence of live lice on day 14. Using intention-to-treat, treatment success rates were 98 percent for the 30-minute malathion

gel ($p < 0.0001$), 97 percent for malathion lotion ($p = 0.006$), and 45 percent for permethrin. Retreatment was highest for permethrin at 70 percent. Adverse events between treatment groups were not significantly different. Malathion gel is not commercially available in the U.S.

permethrin (Nix) and lindane

A randomized, single-blinded, multicenter study of 573 patients with head lice compared efficacy and tolerance of permethrin creme rinse 1% and lindane 1% shampoo.⁷⁸ Both were applied according to the label: permethrin for 10 minutes and lindane for four minutes. At 14 days, 99 percent in the permethrin group were lice-free versus 85 percent of patients on lindane. This was statistically significant. Adverse events were mild and difficult to distinguish from infestation symptoms.

benzyl alcohol (Ulesfia) and placebo

Two randomized, double-blind, vehicle-controlled, multicenter studies evaluated benzyl alcohol 5% lotion in 628 patients six months of age and older with active head lice infestation.⁷⁹ Treatment was applied two times (10 minutes each) separated by one week. Efficacy was assessed as the proportion of subjects who were free of lice 14 days after the final treatment. For evaluation of efficacy, the youngest subject from each household was enrolled in the Primary Treatment Cohort. Other infested household members were enrolled in a Secondary Treatment Cohort and received the same treatment as the youngest subjects. This Secondary Treatment Cohort was not included in the efficacy analysis but was evaluated for safety. Both study one and study two randomized 125 Primary Treatment Cohort subjects each. Fourteen days after the last treatment, both studies combined showed that 75 percent of the subjects treated with benzyl alcohol topical lotion were lice free, compared with 15 percent in the vehicle groups.

Scabies

permethrin and lindane

A randomized, investigator-blinded, multicenter study compared the safety and efficacy of a single, whole-body application of permethrin 5% cream to lindane 1% lotion in 467 patients with scabies.⁸⁰ After 28 days of application, complete resolution was similar in permethrin and lindane groups (91 percent and 86 percent, respectively). Patients had pruritis secondary to scabies in 14 percent of permethrin and 25 percent of lindane groups. New or increased pruritis and mild, transient burning were the most common adverse events and occurred slightly more often in the permethrin group.

permethrin (Elimite) and crotamiton (Eurax)

Permethrin 5% cream was compared for effectiveness to crotamiton 10% cream for the treatment of scabies in a randomized, double-blinded study of 47 children between the ages of two months and five years.⁸¹ Permethrin cured 30 percent of children versus 13 percent for crotamiton after 14 days. Four weeks after treatment, cure rates were 89 percent and 60 percent, respectively.

permethrin, lindane, and crotamiton (Eurax)

A randomized, parallel-group study of 150 patients with scabies compared permethrin 5% to lindane 1% and crotamiton 10%.⁸² Patients were treated for two consecutive nights from neck to toe and then examined at various times for up to four weeks after the last treatment. Cure,

defined as no new lesions and eradication of all original lesions, occurred in 98 percent of patients treated with permethrin, 88 percent of patients treated with crotamiton, and 84 percent treated with lindane. Cure rate was also highest among patients less than 10 years old with permethrin (100 percent) compared to crotamiton (80 percent) or lindane (zero percent). No adverse events were reported in any of the treatment groups.

Meta-analysis

A Cochrane review of randomized trials of pediculicides found permethrin, synergized pyrethrin, and malathion effective in the treatment of lice.⁸³ The review found no evidence that any one pediculicide has greater effect than another. However, the emergence of resistance since these trials were conducted means there is no direct contemporary evidence of the comparative effectiveness of these products. The review emphasizes that the choice of therapy is dependant on local resistance patterns. The review also included studies utilizing physical methods and found them to be ineffective in treating head lice. Comparative studies with agents in this class support this finding.^{84,85} Adverse events reported were minor; however, the reporting quality varied among trials.

A Cochrane review of randomized trials of topical and systemic treatments for scabies found 20 small trials involving 2,392 patients.⁸⁶ Permethrin was more effective than oral ivermectin, crotamiton, and lindane. Permethrin also appeared more effective in reduction of itch persistence than either crotamiton or lindane.

Summary

Topical OTC permethrin and pyrethrins remain effective and recommended in the treatment of head lice, but resistance to these agents has been documented in the U.S. When resistance to permethrin or pyrethrins is documented or in treatment failure, malathion (Ovide) and benzyl alcohol (Ulesfia) are recommended as second-line in patients 24 months or older or in children older than six months, respectively. Higher concentrations of permethrin (Acticin, Elimite) or longer application times for the same agent kill few additional lice. Caution should be used with malathion in order to prevent serious adverse events due to its high alcohol content. Lindane is no longer recommended for the treatment of head lice due to its poor safety and efficacy. Pediculicides are not recommended in children less than two months of age for head lice.

In the treatment of scabies, permethrin (Acticin, Elimite) is the recommended topical agent.

References

- ¹ Ulesfia [package insert]. Atlanta, GA; Sciele Pharma; June 2010.
- ² Eurax [package insert]. Princeton, NJ; Westwood-Squibb; April 2006.
- ³ Lindane [package insert]. Morton Grove, IL; Morton Grove; June 2005.
- ⁴ Ovide [package insert]. Hawthorne, NY; TaroPharma; July 2005.
- ⁵ Permethrin [package insert]. Allegan, MI; Perrigo. Available at: [http://www.perrigo.com/uploadedFiles/Rx/products/P/45802-269\(1\).pdf](http://www.perrigo.com/uploadedFiles/Rx/products/P/45802-269(1).pdf). Accessed November 17, 2010.
- ⁶ www.clinicalpharmacology.com. Accessed November 17, 2010.
- ⁷ www.clinicalpharmacology.com. Accessed November 17, 2010.
- ⁸ Frankowski BL, Bocchini, Jr JA. The Council on School Health and Committee on Infectious Diseases. American Academy of Pediatrics clinical report head lice. Pediatrics. 2010; 126(2):391-403. Available at <http://pediatrics.aappublications.org/cgi/reprint/peds.2010-1308v1>. Accessed November 17, 2010.
- ⁹ Frankowski BL, Bocchini, Jr JA. The Council on School Health and Committee on Infectious Diseases. American Academy of Pediatrics clinical report head lice. Pediatrics. 2010; 126(2):391-403. Available at <http://pediatrics.aappublications.org/cgi/reprint/peds.2010-1308v1>. Accessed November 17, 2010.
- ¹⁰ Meinking TL. Infestations. Curr Probl Dermatol. 1999; 11:73-118.
- ¹¹ Mumcuoglu KY, Klaus S, Kafka D, et al. Clinical observations related to head lice infestation. J Am Acad Dermatol. 1999; 25:248-251.

- ¹² The National Pediculosis Association. Available at <http://www.headlice.org/index.html>. Accessed November 16, 2010.
- ¹³ Roberts RJ. Clinical practice, head lice. *N Engl J Med*. 2002; 346(21):1645-1650.
- ¹⁴ Available at www.cdc.gov/lice/head/epi.html. Accessed November 16, 2010.
- ¹⁵ Flinders DC, De Schweinitz P. Pediculosis and scabies. *Am Fam Physician*. 2004; 69(2):341-348.
- ¹⁶ Frankowski BL, Bocchini, Jr JA. The Council on School Health and Committee on Infectious Diseases. American Academy of Pediatrics clinical report head lice. *Pediatrics*. 2010; 126(2):391-403. Available at <http://pediatrics.aappublications.org/cgi/reprint/peds.2010-1308v1>. Accessed November 17, 2010.
- ¹⁷ Frankowski BL, Bocchini, Jr JA. The Council on School Health and Committee on Infectious Diseases. American Academy of Pediatrics clinical report head lice. *Pediatrics*. 2010; 126(2):391-403. Available at <http://pediatrics.aappublications.org/cgi/reprint/peds.2010-1308v1>. Accessed November 17, 2010.
- ¹⁸ Workowski KA, Berman SM. Sexually transmitted diseases treatment guidelines 2006. Centers for Disease Control and Prevention. *MMWR Recomm Rep*. 2006; 55(RR-11):1-94. Available at www.cdc.gov/mmwr/preview/mmwrhtml/rr5511a1.htm. Also available at <http://www.cdc.gov/std/treatment/2006/ectoparasitic.htm>. Accessed November 16, 2010.
- ¹⁹ Meinking TL, Serrano L, Hard B, et al. Comparative in vitro pediculicidal efficacy of treatments in a resistant head lice population in the United States. *Arch Dermatol*. 2002; 138(2):220-224.
- ²⁰ Elston DM. Drugs used in the treatment of pediculosis. *J Drugs Dermatol*. 2005; 4(2):207-211.
- ²¹ Elston DM. What's eating you? *Pediculus humanus* (head louse and body louse). *Cutis*. 1999; 63(5):259-264.
- ²² Leibold M, Clark L, Levitt J. Therapy for head lice based on life cycle, resistance, and safety considerations. *Pediatrics*. 2007; 119(5):965-974.
- ²³ Burkhart CG. Relationship of treatment-resistant head lice to the safety and efficacy of pediculicides. *Mayo Clin Proc*. 2004; 79(5):661-666.
- ²⁴ Elston DM. Drugs used in the treatment of pediculosis. *J Drugs Dermatol*. 2005; 4(2):207-211.
- ²⁵ Diamnatis SA, Morrell DS, Burkhart CN. Treatment of head lice. *Dermatol Ther*. 2009; 22(4):273-278.
- ²⁶ Heymann WR. Head lice treatments; searching for the path of least resistance. *J Am Acad Dermatol*. 2009; 61(2):323-324.
- ²⁷ Benzyl alcohol lotion for head lice. *Med Lett Drugs Ther*. 2009; 51(1317). Available at <http://medlet.best.secsites.com/restricted/articles/w1317b.html>. Accessed November 17, 2010.
- ²⁸ Hansen RC. Overview: the state of head lice management and control. *Am J Manag Care*. 2004; 10(9):S260-263.
- ²⁹ Wendell K, Rompalo A. Scabies and pediculosis pubis: an update of treatment regimens and general review. *Clin Infect Dis*. 2002; 35(Suppl 2):S146-151.
- ³⁰ Pollack RJ, Kiszewski A, Armstrong P, et al. Differential permethrin susceptibility of head lice sampled in the United States and Borneo. *Arch Pediatr Adolesc Med*. 1999; 153(9):969-973.
- ³¹ Downs AM, Stafford KA, Coles GC. Head lice: prevalence in schoolchildren and insecticide resistance. *Parasitol Today*. 1999; 15(1):1-4.
- ³² Roos TC, Alam M, Roos S, et al. Pharmacotherapy of ectoparasitic infections. *Drugs*. 2001; 61:1067-1088.
- ³³ Heukelbach J, Feldmeier H. Scabies. *Lancet*. 2006; 367(9524):1767-1774.
- ³⁴ Chosidow O. Clinical practices. Scabies. *N Engl J Med*. 2006; 354(16):1718-1727.
- ³⁵ Arlian LG, Runyan RA, Achar S, et al. Survival and infectivity of *Sarcoptes scabiei* var. *canis* and var. *hominis*. *J Am Acad Dermatol*. 1984; 11:210-215.
- ³⁶ Workowski KA, Berman SM. Sexually transmitted diseases treatment guidelines 2006. Centers for Disease Control and Prevention. *MMWR Recomm Rep*. 2006; 55(RR-11):1-94. Available at www.cdc.gov/mmwr/preview/mmwrhtml/rr5511a1.htm. Also available at <http://www.cdc.gov/std/treatment/2006/ectoparasitic.htm>. Accessed November 17, 2010.
- ³⁷ Eurax [package insert]. Princeton, NJ; Westwood-Squibb; June 2003.
- ³⁸ Lindane [package insert]. Morton Grove, IL; Morton Grove; June 2005.
- ³⁹ Ovide [package insert]. Hawthorne, NY; TaroPharma; July 2005.
- ⁴⁰ Permethrin [package insert]. Allegan, MI; Perrigo. Available at: [http://www.perrigo.com/uploadedFiles/Rx/products/P/45802-269\(1\).pdf](http://www.perrigo.com/uploadedFiles/Rx/products/P/45802-269(1).pdf). Accessed November 17, 2010.
- ⁴¹ Leibold M, Clark L, Levitt J. Therapy for head lice based on life cycle, resistance, and safety considerations. *Pediatrics*. 2007; 119(5):965-974.
- ⁴² Ulesfia [package insert]. Atlanta, GA; Sciele Pharma; June 2010.
- ⁴³ Eurax [package insert]. Princeton, NJ; Westwood-Squibb; April 2006.
- ⁴⁴ Lindane [package insert]. Morton Grove, IL; Morton Grove; June 2005.
- ⁴⁵ Ovide [package insert]. Hawthorne, NY; TaroPharma; July 2005.
- ⁴⁶ Permethrin [package insert]. Allegan, MI; Perrigo. Available at: [http://www.perrigo.com/uploadedFiles/Rx/products/P/45802-269\(1\).pdf](http://www.perrigo.com/uploadedFiles/Rx/products/P/45802-269(1).pdf). Accessed November 17, 2010.
- ⁴⁷ Ulesfia [package insert]. Atlanta, GA; Sciele Pharma; June 2010.
- ⁴⁸ Eurax [package insert]. Princeton, NJ; Westwood-Squibb; April 2006.
- ⁴⁹ Lindane [package insert]. Morton Grove, IL; Morton Grove; June 2005.
- ⁵⁰ Ovide [package insert]. Hawthorne, NY; TaroPharma; July 2005.
- ⁵¹ Permethrin [package insert]. Allegan, MI; Perrigo. Available at: [http://www.perrigo.com/uploadedFiles/Rx/products/P/45802-269\(1\).pdf](http://www.perrigo.com/uploadedFiles/Rx/products/P/45802-269(1).pdf). Accessed November 17, 2010.
- ⁵² Ulesfia [package insert]. Atlanta, GA; Sciele Pharma; June 2010.
- ⁵³ Leibold M, Clark L, Levitt J. Therapy for head lice based on life cycle, resistance, and safety considerations. *Pediatrics*. 2007; 119(5):965-974.
- ⁵⁴ Eurax [package insert]. Princeton, NJ; Westwood-Squibb; April 2006.
- ⁵⁵ Lindane [package insert]. Morton Grove, IL; Morton Grove; June 2005.
- ⁵⁶ Ovide [package insert]. Hawthorne, NY; TaroPharma; July 2005.

- ⁵⁷ Permethrin [package insert]. Allegan, MI; Perrigo. Available at: [http://www.perrigo.com/uploadedFiles/Rx/products/P/45802-269\(1\).pdf](http://www.perrigo.com/uploadedFiles/Rx/products/P/45802-269(1).pdf). Accessed November 17, 2010.
- ⁵⁸ Ulesfia [package insert]. Atlanta, GA; Sciele Pharma; June 2010.
- ⁵⁹ Eurax [package insert]. Princeton, NJ; Westwood-Squibb; April 2006.
- ⁶⁰ Lindane [package insert]. Morton Grove, IL; Morton Grove; June 2005.
- ⁶¹ Ovide [package insert]. Hawthorne, NY; TaroPharma; July 2005.
- ⁶² Permethrin [package insert]. Allegan, MI; Perrigo. Available at: [http://www.perrigo.com/uploadedFiles/Rx/products/P/45802-269\(1\).pdf](http://www.perrigo.com/uploadedFiles/Rx/products/P/45802-269(1).pdf). Accessed November 17, 2010.
- ⁶³ Ulesfia [package insert]. Atlanta, GA; Sciele Pharma; June 2010.
- ⁶⁴ Eurax [package insert]. Princeton, NJ; Westwood-Squibb; April 2006.
- ⁶⁵ Lindane [package insert]. Morton Grove, IL; Morton Grove; June 2005.
- ⁶⁶ Ovide [package insert]. Hawthorne, NY; TaroPharma; July 2005.
- ⁶⁷ Permethrin [package insert]. Allegan, MI; Perrigo. Available at: [http://www.perrigo.com/uploadedFiles/Rx/products/P/45802-269\(1\).pdf](http://www.perrigo.com/uploadedFiles/Rx/products/P/45802-269(1).pdf). Accessed November 17, 2010.
- ⁶⁸ Ulesfia [package insert]. Atlanta, GA; Sciele Pharma; June 2010.
- ⁶⁹ Ulesfia [package insert]. Atlanta, GA; Sciele Pharma; April 2009.
- ⁷⁰ Eurax [package insert]. Princeton, NJ; Westwood-Squibb; April 2006.
- ⁷¹ Lindane [package insert]. Morton Grove, IL; Morton Grove; June 2005.
- ⁷² Ovide [package insert]. Hawthorne, NY; TaroPharma; July 2005.
- ⁷³ Permethrin [package insert]. Allegan, MI; Perrigo. Available at: [http://www.perrigo.com/uploadedFiles/Rx/products/P/45802-269\(1\).pdf](http://www.perrigo.com/uploadedFiles/Rx/products/P/45802-269(1).pdf). Accessed November 17, 2010.
- ⁷⁴ www.clinicalpharmacology.com. Accessed November 16, 2010.
- ⁷⁵ www.clinicalpharmacology.com. Accessed November 16, 2010.
- ⁷⁶ Meinking TL, Vicaria M, Eyerdam DH, et al. Efficacy of a reduced application time of Ovide lotion (0.5% malathion) compared to Nix crème rinse (1% permethrin) for the treatment of head lice. *Pediatr Dermatol*. 2004; 21(6):670-674.
- ⁷⁷ Meinking TL, Vicaria M, Eyerdam DH, et al. A randomized, investigator-blinded, time-ranging study of comparative efficacy of 0.5% malathion gel versus Ovide lotion (0.5% malathion) or Nix crème rinse (1% permethrin) used as labeled, for treatment of head lice. *Pediatr Dermatol*. 2007; 24(4):405-411.
- ⁷⁸ Brandenburg K, Deinard AS, DiNapoli J, et al. 1% permethrin cream rinse vs. lindane shampoo in treating pediculosis capitis. *Am J Dis Child*. 1986; 140(9):894-896.
- ⁷⁹ Ulesfia [package insert]. Atlanta, GA; Sciele Pharma; June 2010.
- ⁸⁰ Schultz MW, Gomez M, Hansen RC, et al. Comparative study of 5% permethrin cream and 1% lindane lotion for the treatment of scabies. *Arch Dermatol*. 1990; 126(2):167-170.
- ⁸¹ Taplin D, Meinking TL, Chen JA, et al. Comparison of crotamiton 10 % cream (Eurax) and permethrin 5% cream (Elimite) for the treatment of scabies in children. *Pediatr Dermatol*. 1990; 7(1):67-73.
- ⁸² Amer M. el-Gharib I. Permethrin versus crotamiton and lindane in the treatment of scabies. *Int J Dermatol*. 1992; 31(5):357-358.
- ⁸³ Dodd CS. Withdrawn: interventions for treating headlice. *Cochrane Database Syst Rev*. 2007; (4):CD001165. Update of: *Cochrane Database Syst Rev*. 2001; (3):CD001165.
- ⁸⁴ Roberts RJ, Casey D, Morgan DA, et al. Comparison of wet combing with malathion for treatment of head lice in the UK: a pragmatic randomized controlled trial. *Lancet*. 2000; 356(9229):540-544.
- ⁸⁵ Meinking TL, Clineschmidt CM, Chen C, et al. An observer-blinded study of 1% permethrin creme rinse with and without adjunctive combing in patients with head lice. *J Pediatr*. 2002; 141(5):665-670.
- ⁸⁶ Strong M, Johnstone PW. Interventions for treating scabies. *Cochrane Database Syst Rev*. 2007; (3):CD000320.