Therapeutic Class Overview
Scabicides and Pediculicides

Therapeutic Class

- **Overview/Summary:** The agents indicated for the management of scabies and head lice are listed in Table 1. All of these agents are Food and Drug Administration (FDA)-approved for the treatment of head lice with the exception of crotamiton (Eurax®), which is only indicated to treat scabies.[1-8] The scabicides and pediculicides have a neurotoxic effect on lice and scabies, resulting in periods of central nervous system hyperexcitation, ultimately resulting in paralysis and death of the parasite.[1-8] Benzyl alcohol (Ulesfia®) disables the breathing structure of the lice, resulting in asphyxiation rather than neuroexcitation.[1] The challenge of complete eradication of the infestation with a single treatment results from the fact that the neurotoxic insecticides rely on the nervous system to exert their effect; therefore, newborn larvae are not susceptible to these agents as they do not have intact nervous systems for several days after eggs are hatched. Pyrethrins (RID®) and permethrin (Nix®) are pediculicidal, but not ovicidal, and require nit combing and retreatment in seven to 10 days. Resistance to pyrethrins and permethrin has been reported to be increasing in the United States. Benzyl alcohol is not ovicidal and also requires a second treatment, but resistance is unlikely due to its unique mechanism of action. Malathion is both pediculicidal and ovicidal, but must be applied for eight to 12 hours, and is highly flammable. Lindane is neurotoxic and is not recommended as an initial treatment option.[9] Ivermectin (Sklice®) and spinosad (Natroba®) are pediculicidal but not ovicidal. According to the manufacturer, spinosad is the first FDA-approved head lice treatment that does not require nit combing following treatment.[3,7] Although spinosad is not ovicidal, it is not metabolized and as a result, is still present and able to exert its effect when the lice larvae nervous system does develop. This potentially prevents the need for a repeat application. Ivermectin lotion is approved as a single application product only.[7] Lindane, malathion, permethrin, piperonyl butoxide and pyrethrins and spinosad are available generically, while permethrin, and piperonyl butoxide and pyrethrins products are also available over-the-counter in various topical formulations including creams, lotions and shampoos.

Table 1. Current Medications Available in the Therapeutic Class[1-8,10]

Generic (Trade Name)	Food and Drug Administration Approved Indications	Dosage Form/Strength	Generic Availability
Single-Entity Products			
Benzyl alcohol (Ulesfia®)	Treatment of head lice	Lotion: 5% (227 g/bottle)	-
Crotamiton (Eurax®)	Treatment of scabies	Cream: 10% (2 oz/ tube) Lotion: 10% (2 oz/bottle, 16 oz/bottle)	-
Ivermectin (Sklice®)	Treatment of head lice	Lotion: 0.5% (4 oz/tube)	-
Lindane*	Treatment of head and pubic lice and scabies	Lotion: 1% (2 oz/bottle) Shampoo: 1% (2 oz/bottle)	✔
Malathion (Ovide®*)	Treatment of head lice	Lotion: 0.5% (2 oz/ bottle)	✔
Permethrin*† (Acticin®, Nix Complete Lice System®*†, Nix Crème Rinse®*†)	Treatment of head lice and scabies	Cream: 5% (2 oz/tube)	✔

Generic (Trade Name)	Food and Drug Administration Approved Indications	Dosage Form/Strength	Generic Availability
		Liquid: 1% (2 oz/bottle) Lotion: 1% (2 oz/bottle, 4 oz/bottle)	
Spinosad (Natroba®*)	Treatment of head lice	Topical Suspension: 0.9% (4 oz/bottle)	✔
Combination Products			
Piperonyl butoxide and pyrethrins*† (Licide Complete Lice Treatment Kit®*†, Pronto®*†, RID®*†)	Treatment of head, body and pubic lice	Gel: 4/0.33% (each kit) Shampoo: 4/0.33% (each kit) Solution: 4/0.33% (each kit)	✔

*Generic available in one dosage or strength.
†Over-the-counter product is available in at least one dosage form or strength.

Evidence-based Medicine

- In two, randomized, active-controlled trials in patients with an active head lice infestation, a greater proportion of patients were lice-free 14 days following treatment with spinosad alone compared to patients who received permethrin plus nit combing (*P*<0.001 for both trials).[11]
- The combined results of two identical, vehicle-controlled trials (N=765) in patients six months and older with head lice showed that significantly more patients treated with ivermectin lotion were lice-free on day two (94.9 vs 31.3%), day eight (85.2 vs 20.8%) and remained lice-free through day 15 (73.8 vs 17.6%; *P*<0.001 for each day) compared to the vehicle group.[12]
- In two studies comparing benzyl alcohol to its vehicle, the absolute difference in treatment success rate in study one was 71.4% in favor of benzyl alcohol (95% confidence interval [CI], 61.8 to 85.7) and 48.8% (95% CI, 31.1 to 62.0) in study two, again in favor of benzyl alcohol. Benzyl alcohol was associated with a lower risk of treatment failure in both studies (*P*<0.001 for both).[13]
- For the treatment of lice, permethrin has demonstrated a higher rate of treatment success compared to lindane, following a single application.[14-17] Compared to the combination of pyrethrins and piperonyl butoxide, permethrin was more efficacious several days following treatment; however, one study found the agents to be equally effective at 14 days following treatment (*P*>0.01).[18,19] In multiple studies, malathion has been reported to be pediculicidal and ovicidal when compared to permethrin.[20,21]
- In studies comparing various topical agents for the treatment of scabies, a higher cure rate has been demonstrated with permethrin compared to crotamiton and lindane.[22-27] In the largest study completed (N=467), Schultz et al reported that there was a trend towards a higher cure rate with permethrin treatment compared to lindane; however, the difference was not statistically significant.[23]

Key Points within the Medication Class

- According to Current Clinical Guidelines:
  - Head lice treatment can be initiated with permethrin 1% or pyrethrins when resistance to these products is not suspected. These agents are available over-the-counter without a prescription.[27,28]
  - Malathion 0.5% can be used in people who are ≥24 months of age when resistance to permethrin or pyrethrins is documented or when treatment with these products fails despite their correct use. Due to the high alcohol concentration of the product it is highly flammable.[27,28]

  - Permethrin is the most studied pediculicide and is the least toxic to humans. Permethrin is less allergenic than pyrethrins and does not cause allergic reactions in individuals with plant allergies.[28]
  - Lindane has low ovicidal activity (30 to 50% of eggs are not killed), and resistance has been reported worldwide for many years. For these reasons, it should be used cautiously. The Food and Drug Administration (FDA) has warned that incorrect use of lindane can be neurotoxic and its use should be restricted to patients for whom prior treatments have failed or in those patients who cannot tolerate safer medications.[27,28]
  - Lindane should not be used to treat premature infants, persons with the human immunodeficiency virus, seizure disorders, women who are pregnant or breast-feeding, persons who have very irritated skin or sores where the lindane will be applied, infants, children, the elderly, and persons who weigh <110 pounds.[27,28]
  - Permethrin is the drug of choice for the treatment of scabies. Two (or more) applications may be necessary to eliminate all mites, particularly when treating crusted (Norwegian) scabies.
  - Crotamiton is approved for the treatment of scabies in adults but is frequently associated with treatment failure.[29]
  - Lindane is not recommended as a first-line therapy for the treatment of scabies due to its potential for toxicity with frequent or incorrect use. Lindane should be restricted to patients who have failed recommended therapies or who cannot tolerate recommended treatments.[29]
- Other Key Facts:
  - All recommended first-line therapies are available generically in at least one strength or formulation.[10]
  - According to the manufacturer, spinosad is the first FDA-approved head lice treatment that does not require nit combing following treatment.[30]
  - Ivermectin is approved for use as a single application only and is not indicated for retreatment.[3]
  - Reasons for treatment failure with the topical scabicide and pediculicide products include misdiagnosis, noncompliance, failure to follow instructions correctly, not enough pediculicide applied, reinfestation, and resistance. If resistance is suspected, retreatment should be with a different chemical entity than initially used.[31]

References

1. Ulesfia® [package insert]. Atlanta (GA): Shionogi Pharma Inc.; 2012 Jul.
2. Eurax® [package insert]. Jacksonville (FL): Ranbaxy; 2009 Jul.
3. Sklice® [package insert]. Swiftwater (PA): Sanofi Pasteur Inc.; 2012 Feb.
4. Lindane® [package insert]. Morton Grove (IL): Morton Grove Pharmaceuticals Inc.; 2005 Jun.
5. Ovide® [package insert]. Hawthome (NY): Taro Phrmaceuticals U.S.A., Inc.; 2011 Nov.
6. Permethrin: drug information. In: Rose BD, ed. UpToDate [database on the Internet]. Waltham, MA: UpToDate; 2013. [cited 2013 Jun 13]. Available from: http://www.uptodate.com/contents/permethrin-drug-information?source=search_result&search=Nix&selectedTitle=1%7E150
7. Natroba® [package insert]. Carmel (IN): ParaPro LLC.; 2011 Jan.
8. Pyrethrins: drug information. In: Rose BD, ed. UpToDate [database on the Internet]. Waltham, MA: UpToDate; 2013. [cited 2013 Jun 13]. Available from: http://www.uptodate.com/contents/pyrethrins-drug-information?source=search_result&search=pyrethrin&selectedTitle=1%7E11.
9. Spinosad (Natroba) topical suspension for head lice. Med Lett Drugs Ther. 2011 Jun 27;53(1367):50-1.
10. Drug Facts and Comparisons 4.0 [database on the Internet]. St. Louis: Wolters Kluwer Health, Inc.; 2013 [cited 2013 Jun 13]. Available from: http://online.factsandcomparisons.com.
11. Stough D, Shellabarger MS, Quiring J, Gabrielsen AA. Efficacy and safety and spinosad and permethrin crème rinses for pediculosis capitis (head lice). Pediatrics. 2009;124:389e-95e.
12. Pariser DM, Meinking TL, Bell M, Ryan WG. Topical 0.5% ivermectin lotion for treatment of head lice. N Engl J Med. 2012 Nov;367(18):1687-93.
13. Meinking TL, Villar ME, Vicaria M, Eyerdam DH, Paquet D, Mertz-Rivera K, et al. The clinical trials supporting benzyl alcohol lotion 5% (Ulesfia): a safe and effective topical treatment for head lice (pediculosis humanus capitis). Pediatr Dermatol. 2010 Jan-Feb;27(1):19-24.
14. Brandenburg K, Deinard AS, DiNapoli J, Englender SJ, Orthoefer J, Wagner D.1% permethrin cream rinse vs. 1% lindane shampoo in treating pediculosis capitis. Am J Dis Child. 1986; 140:894-6.
15. Taplin D, Meinking TL, Castillero PM, Sanchez R. Permethrin 1% creme rinse for the treatment of Pediculus humanus var capitis infestation. Pediatr Dermatol. 1986;3:344-8.
16. Bowerman JG, Gomez MP, Austin RD, Wold DE. Comparative study of permethrin 1% creme rinse and lindane shampoo for the treatment of head lice. Pediatr Infect Dis J. 1987;6:252-5.

17. Kalter DC, Sperber J, Rosen T, Matarasso S. Treatment of pediculosis pubis. Clinical comparison of efficacy and tolerance of 1% lindane shampoo vs. 1% permethrin creme rinse. Arch Dermatol. 1987;123:1315-9.
18. Carson DS, Tribble PW, Weart CW. Pyrethrins combined with piperonyl butoxide (RID) vs. 1% permethrin (NIX) in the treatment of head lice. Am J Dis Child. 1988;142:768-9.
19. DiNapoli JB, Austin RD, Englender SJ, Gomez MP, Barrett JF. Eradication of head lice with a single treatment. Am J Public Health. 1988;78:978-80.
20. Roberts RJ, Casey D, Morgan DA, Petrovic M. Comparison of wet combing with malathion for treatment of head lice in the UK: a pragmatic randomized controlled trial. Lancet. 2000;356:540-4.
21. Meinking TL, Vicaria M, Eyerdam DH, Villar ME, Reyna S, Suarez G. Efficacy of a reduced application time of ovide lotion (malathion) compared to nix crème rinse (1% permethrin) for the treatment of head lice. Pediatric Dermatology. 2004; 21(6);670-4.
22. Haustein UF, Hlawa B. Treatment of scabies with permethrin vs lindane and benzyl benzoate. Acta Derm Venereol. 1989;69:348-51.
23. Schultz MW, Gomez M, Hansen RC, Mills J, Menter A, Rodgers H, et al. Comparative study of 5% permethrin cream and 1% lindane lotion for the treatment of scabies. Arch Dermatol. 1990;126:167-70.
24. Zargari O, Golchai J, Sobhani A, Dehpour AR, Sadr-Ashkevari S, Alizadeh N, et al. Comparison of the efficacy of topical 1% lindane vs. 5% permethrin in scabies: A randomized, double-blind study. Indian J Dermatol Venereol Leprol. 2006;72;33-6.
25. Taplin D, Meinking TL, Porcelain SL, Castilero PM, Chen JA. Permethrin 5% dermal cream: a new treatment for scabies. J Am Acad Dermatol. 1986;15:995-1001.
26. Taplin D, Meinking TL, Chen JA., Sanchez R. Comparison of crotamiton 10% cream (Eurax) and permethrin 5% cream (Elimite) for the treatment of scabies in children. Pediatr Dermatol. 1990;7:67-73.
27. Amer M, el-Garib I. Permethrin vs crotamiton and lindane in the treatment of scabies. Int J Dermatol. 1992;31:357-8.
28. Treatment of Head Lice. Centers for Disease Control and Prevention. 2010. [cited 2013 Jun 13]. Available at: http://www.cdc.gov/lice/head/treatment.html.
29. Frankowski BL, Bocchini JA Jr; Council on School Health and Committee on Infectious Diseases. Head lice. Pediatrics. 2010 Aug;126(2):392-403. [cited 2013 Jun 13] Available at: http://pediatrics.aappublications.org/content/early/2010/07/26/peds.2010-1308.
30. Treatment of Scabies. Centers for Disease Control and Prevention. 2010. [cited 2013 Jun 13]. Available at: http://www.cdc.gov/parasites/scabies/treatment.html.
31. ParaPRO Announces FDA Approval of Natroba™ for Treatment of Head Lice [press release on the Internet]. Carmel (IN): ParaPro LLC; 2011 Jan 18 [cited 2013 Jun 13]. Available from: http://www.parapro.com/documents/Natroba_Approval_PressRelease.pdf.
32. Wendel K, Rompalo A. Scabies and pediculosis pubis: an update of treatment regimens and general review. Clin Infect Dis. 2002;35(Suppl 2):S146-51.

Therapeutic Class Review
Scabicides and Pediculicides

Overview/Summary

Scabies and pediculosis are infestations of the skin caused by ectoparasites. Scabies is caused by the parasitic mite Sarcoptes scabiei and often results in an intense prutitic eruption and itching. Pediculi, or lice, can cause infestations either on the head (Pediculus humanus capitis), body (Pediculus humanus corporis) or the pubic region (Phthirus pubis). These skin conditions are common causes of skin rash and pruritus.[1,2] Head lice infestation crosses all social and geographic boundaries and generally affects children, primarily females, aged three to 12 years.[3] Scabies occur in both sexes, at all ages, and in all ethnic and socioeconomic groups; however, one epidemiologic study reported a higher prevalence in urban areas among women and children.[4,5] The ideal agent for the treatment of head lice is one with high pediculicidal (capable of killing lice) and ovicidal (capable of killing eggs) activity with minimal toxicity.[6]

The topical agents indicated for the management of scabies and head lice are listed in Table 1. All of the agents are Food and Drug Administration (FDA)-approved for the treatment of head lice with the exception of crotamiton (Eurax®), which is only indicated to treat scabies.[7-14] The pediculicidal effects of these agents result from their neurotoxic effects on lice.[8-14] These agents cause periods of central nervous system hyperexcitation, resulting in paralysis and ultimately death of the lice. Benzyl alcohol (Ulesfia®) disables the breathing structure of the lice, resulting in asphyxiation rather than neuroexcitation.[7] Neurotoxic insecticides rely on the nervous system to exert their effect; therefore, newborn larvae are not susceptible to these agents since they do not develop a nervous system for several days after hatching. This presents a challenge for eliminating lice with a single treatment because the infestation typically includes lice from all stages of the life cycle, including newly hatched eggs.

Pyrethrins (RID®) and permethrin (Nix®) are pediculicidal, but not ovicidal, and therefore require nit combing and retreatment in seven to 10 days to eradicate the infestation. Benzyl alcohol is not ovicidal and also requires a second treatment, but resistance is unlikely due to its unique mechanism of action. Malathion is both pediculicidal and ovicidal, but it is malodorous, requires eight to 12 hours of application and is highly flammable. Lindane is neurotoxic to humans and is not recommended for initial treatment.[10] Two of the newer agents approved by the FDA are ivermectin (Sklice®) and spinosad (Natroba®). Spinosad and ivermectin are pediculicidal but not ovicidal. According to the manufacturer, spinosad does not require nit combing after treatment.[13] Although spinosad is not ovicidal, it is not metabolized and as a result, is still present and able to exert its effect when the lice larvae nervous system does develop.[13] This potentially prevents the need for a repeat application. Ivermectin lotion is approved as a single application product only.[9]

Lindane, malathion, permethrin and piperonyl butoxide and pyrethrins and spinosad products are available generically, while permethrin, and piperonyl butoxide and pyrethrins products are also available over-the-counter. All agents approved for the treatment of scabies are prescription only products.[16] Although some data suggest a growing resistance to permethrin in the United States, both the Centers for Disease Control and Prevention as well as the American Academy of Pediatrics continue to recommend permethrin as first-line antiparasitic therapy for treatment of both lice and scabies. For the treatment of head lice, therapy should be initiated with permethrin 1% or pyrethrins when resistance is not suspected. Malathion may be used in patients who are two years of age or older when resistance to permethrin or pyrethrins is documented or when treatment with these products fails despite their correct use. Benzyl alcohol may be a useful alternative due to its unique mechanism of action. Lindane, while still widely used, is considered second-line therapy due to toxicity risks.[17-20]

Medications

Table 1. Medications Included Within Class Review[7-14,16]

Generic Name (Trade name)	Medication Class	Generic Availability
Single-Entity Agents		
Benzyl alcohol (Ulesfia®)	Scabicide and pediculicide	-
Crotamiton (Eurax®)	Scabicide and pediculicide	-
Ivermectin (Sklice®)	Scabicide and pediculicide	-
Lindane	Scabicide and pediculicide	✔
Malathion (Ovide®*)	Scabicide and pediculicide	✔
Permethrin*† (Acticin®, Nix Complete Lice System®*†, Nix Crème Rinse®*†)	Scabicide and pediculicide	✔
Spinosad (Natroba®*)	Scabicide and pediculicide	✔
Combination Products		
Piperonyl butoxide and pyrethrins*† (Licide Complete Lice Treatment Kit®*†, Pronto®*†, RID®*†)	Scabicide and pediculicide	✔

*Generic available in one dosage or strength.
†Over-the-counter product is available in at least one dosage form or strength.

Indications

Table 2. Food and Drug Administration-Approved Indications[7-14,16]

Drug(s)	Scabies	Head Lice	Head and Pubic Lice	Head, Body, and Pubic Lice
Single-Entity Agents				
Benzyl alcohol		✔ *		
Crotamiton	✔			
Ivermectin		✔ *		
Lindane	✔ †		✔ ‡	
Malathion		✔		
Permethrin	✔ §	✔ ‖		
Spinosad		✔ ¶		
Combination Products				
Piperonyl butoxide and pyrethrins				✔

* In patients ≥6 months of age.
†Lindane lotion is reserved for patients who cannot tolerate or have failed first-line treatment with safer medications for the treatment of scabies.
‡Lindane shampoo is reserved for patients who cannot tolerate or have failed first-line treatment with safer medications for the treatment of head or public lice.
§ Permethrin cream is indicated for the treatment of scabies.
‖ Permethrin lotion/cream rinse and liquid are indicated for the treatment of head lice.
¶ In patients ≥4 years of age.

In addition to its Food and Drug Administration-approved indication, permethrin may also be used off-label in the treatment of papulopustular rosacea, and crotamiton has been used in the treatment of head lice.[15]

Pharmacokinetics

Table 3. Pharmacokinetics[16,21]

Generic Name	Bioavailability (%)	Absorption (%)	Renal Excretion (%)	Active Metabolites	Serum Half-Life (hours)
Single-Entity Agents					
Benzyl alcohol	Not reported	Not reported	Not reported	Not reported	Not reported
Crotamiton	Not reported	Not reported	Not reported	Not reported	Not reported

Generic Name	Bioavailability (%)	Absorption (%)	Renal Excretion (%)	Active Metabolites	Serum Half-Life (hours)
Ivermectin	Not reported	Not reported	Not reported	Not reported	Not reported
Lindane	Not reported	10	Not reported	Not reported	18
Malathion	Not reported	8	Not reported	Not reported	1.2 to 7.6
Permethrin	Not reported	≤2	Not reported	Not reported	Not reported
Spinosad*	Not reported	Not reported	Not reported	Not reported	Not reported
Combination Products					
Piperonyl butoxide and pyrethrins	Not reported	Not reported	Not reported	Not reported	Not reported

* In a pharmacokinetic study, the plasma spinosad concentrations in samples obtained from 14 patients with head lice, were below the limit of detection following a single 10 minute topical treatment. In addition, the bioavailability of benzyl alcohol, which is contained in the topical suspension, is unknown as plasma concentrations were not determined in the evaluated subjects.[13]

Clinical Trials

Clinical studies evaluating the safety and efficacy of the topical pediculicide and scabicide products for their respective Food and Drug Administration-approved indications are described in Table 4.[22-47]

Benzyl alcohol has been evaluated in two multicenter, randomized, double-blind, vehicle-controlled studies in patients (six months and older) with an active head lice infestation (N=628). In both studies, two applications of benzyl alcohol were associated with a significantly greater chance of treatment success (zero live lice 14 days following final treatment), compared to vehicle (*P*<0.001). The absolute difference in treatment success rates in study one was 71.4% in favor of benzyl alcohol (95% confidence interval [CI], 61.8 to 85.7) and 48.8% (95% CI, 31.1 to 62.0) in study two, again in favor of benzyl alcohol. In both studies, there was a lower incidence of treatment failure associated with benzyl alcohol compared to vehicle (3.3 vs 83.6% and 14.3 vs 60.7% in studies one and two, respectively; *P*<0.001 for both).[33]

In studies comparing various topical agents for the treatment of scabies, a higher cure rate has been reported with permethrin compared to crotamiton and lindane.[22-27] In the largest study completed (N=467), Schultz et al reported that there was a trend towards a higher cure rate with permethrin compared to lindane, however the difference was not statistically significant.[23] Both lindane and permethrin have also been compared to ivermectin for the treatment of scabies. While a study by Madan et al demonstrated a lower cure rate after four weeks with lindane compared to ivermectin (44.44 vs 82.60%; *P* value not reported), Chouelea and colleagues reported similar efficacy between the two agents.[28,29] Results from another study found that after a single application, permethrin was associated with a higher cure rate compared to ivermectin (95 vs 70%; *P* value not reported).[30]

Permethrin has demonstrated a higher rate of treatment success compared to lindane in the treatment of lice, when both were administered as a single application.[35-38] Compared to the combination of pyrethrins and piperonyl butoxide, permethrin was more efficacious several days following treatment; however, one study found the agents to be equally effective after 14 days (*P*>0.01).[39,40] In multiple studies, malathion has been reported to be pediculicidal and ovicidal when compared to permethrin.[41,44]

The combined results of two identical, vehicle-controlled trials (N=765) in patients six months and older with head lice showed that significantly more patients treated with ivermectin lotion were lice-free on day two (94.9 vs 31.3%), day eight (85.2 vs 20.8%) and remained lice-free through day 15 (73.8 vs 17.6%; *P*<0.001 for each day) compared to the vehicle group.[34]

Spinosad has been evaluated in two randomized, active-controlled trials (N=1,038) of patients with an active head lice infestation. Patients received spinosad without nit combing or permethrin 1% topical solution with nit combing. Fourteen days following treatment, the spinosad without nit combing treatment arm had a greater proportion of lice-free patients compared to permethrin with nit combing (*P*<0.001 for both trials). Moreover, the majority of patients treated with spinosad required only one course of treatment, compared to the majority of permethrin-treated patients who required two courses of treatment (*P* values not reported).[47]

Table 4. Clinical Trials

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
Scabies				
Haustein et al[22] Lindane (1 and 0.3%) vs permethrin (5 and 2.5%) vs benzyl benzoate (20 and 10%)*	AC, OL Adults and children with scabies	N=194 3 weeks	Primary: Efficacy (cure rate) Secondary: Adverse events	Primary: While permethrin and benzyl benzoate were 100% effective, lindane was 92% effective (treatment failures in three adults and two children). Lindane was significantly less effective compared to permethrin and benzyl benzoate (*P*<0.025). Secondary: Benzyl benzoate had more immediate (22%) and late (42%) adverse events compared to the other treatment arms.
Schultz et al[23] Lindane lotion 1% vs permethrin cream 5%	AC, MC, RCT Patients with scabies who had otherwise normal skin in non-infested areas	N=467 1 month	Primary: Efficacy (cure rate) Secondary: Adverse events	Primary: One hundred and eighty one of 199 (91%) and 177 of 205 (86%) patients treated with permethrin and lindane, respectively had complete resolution after treatment (*P*=0.18). Secondary: The most frequent adverse events were transient burning or stinging and new or increased pruritus. Events were more frequent following permethrin treatment and appeared to be related to the severity of the infestation.
Zargari et al[24] Lindane cream 1% vs permethrin cream 5%	AC, DB, RCT Patients ≥5 years of age with scabies	N=99 2 weeks	Primary: Efficacy (cure rate) Secondary: Not reported	Primary: After two weeks, permethrin provided an improvement in 84.6% of patients compared to 48.8% of patients receiving lindane (*P*<0.0001). Secondary: Not reported
Taplin et al[25] Lindane lotion 1%	AC, RCT Patients with microscopically	N=23 1 month	Primary: Efficacy (cure rate)	Primary: Three of 23 (13%) patients who received lindane were free of scabies at study midpoint (two weeks). After one month, 15 of 23 (65%) patients who received lindane were considered cured (*P* value not

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
vs permethrin cream 5%	confirmed scabies		Secondary: Not reported	reported). At study midpoint (two weeks) 11 of 23 patients who received permethrin were considered cured (48%). After one month, two patients who received permethrin had scabies resulting in a cure rate of 91% (*P*<0.025). Secondary: Not reported
Taplin et al[26] Permethrin cream 5% vs crotamiton cream 10%	AC, DB, RCT Treatment of scabies in children 2 months to 5 years of age	N=47 1 month	Primary: Efficacy (cure rate) Secondary: Not reported	Primary: Fourteen of 47 (30%) children were considered cured two weeks after permethrin treatment compared to only 6 of 47 (13%) subjects treated with crotamiton (*P*<0.0001). Four weeks following treatment, a higher percentage of patients treated with permethrin were considered cured compared to patients who received crotamiton (89 vs 60%; *P*=0.002). Secondary: Not reported
Amer et al[27] Lindane 1% vs permethrin 5% vs crotamiton 10%	AC, RCT Patients microscopically diagnosed with scabies	N=150 1 month	Primary: Efficacy (cure rate) Secondary: Adverse events	Primary: After four weeks of treatment, the cure rates were 84, 98 and 88% for patients receiving lindane, permethrin and crotamiton treatment, respectively (*P* values not reported). Secondary: No adverse events were reported.
Chouela et al[28] Lindane solution 1%	AC, DB, DD, PG, PRO, RCT Patients	N=53 1 month	Primary: Clinical healing Secondary:	Primary: At day 15 following treatment, 14 patients (74%) in the ivermectin group showed healing of their scabies compared to 13 patients (54%) in the lindane group (*P*=0.22).

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
vs ivermectin in a single oral dose of 150 to 200 µg/kg of body weight	diagnosed with scabies		Adverse events	There was no difference in efficacy between lindane and ivermectin treatments after 29 days (95 vs 96%; *P*>0.99). Secondary: Adverse events from the treatments were few, mild and transient.
Madan et al[29] Lindane lotion 1% vs ivermectin in a single oral dose of 200 µg/kg body weight	AC, RCT Patients with scabies	N=200 1 month	Primary: Efficacy (cure rate) Secondary: Adverse events	Primary: In the ivermectin group, 82.60% of the patients showed marked improvement after four weeks compared to 44.44% of patients in the lindane group (*P*<0.0001). Secondary: One severe headache was reported in the ivermectin treatment group.
Usha et al[30] Permethrin cream 5% vs ivermectin in a single oral dose of 200 µg/kg body weight	AC, RCT Patients ≥5 years of age with microscopically diagnosed scabies and family contacts	N=85 2 months	Primary: Efficacy (cure rate) Secondary: Not reported	Primary: A cure rate of 70% was reported after a single dose of ivermectin, and increased to 95% following two doses at a two-week interval. Two weeks following a single application, permethrin was associated with a significantly higher rate of symptomatic improvement compared to oral ivermectin (97.8 vs 75.0%; *P*<0.001). All patients were considered to have been cured within two months following treatment. Secondary: Not reported
Goldust et al[31] Permethrin cream 5% vs ivermectin in a single oral dose of 200 µg/kg body weight	AC, RCT Patients aged 2 to 84 years of age with a diagnosis of scabies and family contacts	N=242 4 weeks	Primary: Efficacy (cure rate) Secondary: Not reported	Primary: Two weeks following treatment, a similar proportion of patients treated with permethrin cream or oral ivermectin experienced a cure (92.5 vs 85.9%; *P*=0.42). Twenty six patients who had not improved were crossed over to the other treatment group. When crossed over, seven patients in the permethrin 5% group who experienced treatment failure continued to have severe itching when treated with ivermectin. In contrast, all 17

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
				patients not responding to ivermectin who were then treated with permethrin showed improvement in itching and skin lesions. Secondary: Not reported
Chhaiya et al[32] Permethrin cream 5% vs ivermectin in a single oral dose of 200 µg/kg body weight vs ivermectin lotion 1%	AC, OL, PG, RCT Patients 5 to 80 years of age with clinically-diagnosed scabies and presence of typical scabei lesions like papules, nodules, or vesicles at classical sites	N=315 4 weeks	Primary: Efficacy (cure rate) Secondary: Complete relief of pruritus	Primary: Significantly fewer patients treated with oral ivermectin compared to ivermectin lotion or permethrin cream were cured at one week (30 vs 69.3 and 74.8%, respectively; *P*<0.05) and two weeks (63 vs 100 and 99%, respectively; *P*<0.05). There was no statistically significant difference in cure rates between the three treatments by three or four weeks following treatment (*P*>0.05 for both). Secondary: Patients treated with ivermectin lotion and permethrin cream experienced significantly higher pruritus cure rates compared to oral ivermectin at two (*P*<0.05) and three weeks (*P*<0.05). By week four, 95, 99 and 98% of patients treated with oral ivermectin, ivermectin lotion and permethrin cream, respectively, were cured of pruritus (*P*>0.05).
Head, Body, or Pubic Lice				
Meinking et al[33] Benzyl alcohol lotion 5% vs vehicle	2 DB, MC, PC, RCT The youngest member of each participating household (≥6 months of age) with active cases of head lice (3 live lice)	N=250 22 days	Primary: Treatment success (no live lice) 14 days following final treatment Secondary: Treatment failure assessed one day following second treatment	Primary: Benzyl alcohol treatment was associated with a significantly greater chance of treatment success (absence of live lice 14 days after the final treatment), compared to vehicle in both studies (*P*<0.001). The absolute difference in treatment success rates in study one was 71.4% in favor of benzyl alcohol (95% CI, 61.8 to 85.7). In study two, the difference of overall treatment success rate between the two treatment groups was 48.8% in favor of benzyl alcohol (95% CI, 31.1 to 62.0). Secondary: Treatment failure one day following the second treatment was significantly lower with benzyl alcohol compared to vehicle. In study one, 3.3% of patients receiving benzyl alcohol were considered treatment failures, compared to 83.6% in the vehicle group (*P*<0.001).

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
				In study two, 14.3% of patients receiving benzyl alcohol experienced a treatment failure, compared to 60.7% of vehicle-treated patients (*P*<0.001).
Pariser et al[34] Ivermectin lotion 0.5% vs vehicle	2 DB, MC, PC, RCT Patients ≥6 months of age with head lice who agreed not to use any other louse treatment, comb out nits, or cut or chemically treat hair	N=765 15 days	Primary: Number of index patients who were louse-free by day two and remained louse-free through days eight and 15 (ITT population) Secondary: Number of index patients plus all enrolled household members who were louse-free by day two and remained louse-free through days eight and 15 (extended ITT population) and safety	Primary: Significantly more patients treated with ivermectin were free of live lice at the first post-application observation on day two and at the subsequent observations through day 15 (*P*<0.001 for all). The combined ITT analysis showed that significantly more patients in the ivermectin group were lice-free on day two (94.9 vs 31.3%), day eight (85.2 vs 20.8%) and day 15 (73.8 vs 17.6%) compared to the vehicle group (*P*<0.001 for each day). Secondary: Results were consistent when cure rates in the extended ITT populations were analyzed (95.5 vs 35.3% at day two, 88.6 vs 26.2% at day eight and 78.7 vs 22.2% at day 15; *P*<0.001 for all comparisons). Pruritus, excoriation and erythema were the most common adverse events, occurring in >1% in the vehicle group and <1% in the ivermectin group. There was one severe adverse event (pain in an extremity with vehicle) and no serious adverse events. All other adverse events were mild to moderate. The frequency and severity of adverse events were similar in the two study groups and across age groups. Ocular irritation was noted in seven patients in the ivermectin group and five in the vehicle-control group on day two.
Brandenberg et al[35] Lindane shampoo 1% vs permethrin cream rinse 1%	MC, RCT, SB Patients with head lice	N=573 (559 assessable for tolerance; 508 assessable for efficacy)	Primary: Efficacy (cure rate) Secondary: Tolerance	Primary: At 14 days following treatment, 99% of patients who received permethrin were lice-free compared to 85% of patients treated with lindane (*P*<0.001). Secondary: Adverse events reported with both treatments, were infrequent, mild,

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
		2 weeks		and usually difficult to distinguish from the symptoms of head lice infestation.
Taplin et al[36] Permethrin crème rinse 1% vs lindane shampoo 1% vs placebo	DB, PC, RCT Patients with head lice	N=93 2 weeks	Primary: Efficacy (cure rate) Secondary: Safety	Primary: Ninety seven percent of patients treated with permethrin were lice-free after 14 days compared to 6% of placebo-treated patients (*P*<0.001) and 43% of the lindane-treated patients. Permethrin was 70% ovicidal compared to 45 and 14% for lindane and placebo, respectively (*P*<0.001). Secondary: No adverse events were reported during this study.
Bowerman et al[37] Lindane shampoo 1% vs permethrin crème rinse 1%	RCT Patients with head lice in the Nezahualcoyotl community of Mexico city (296 family groups)	N=1,040 2 weeks	Primary: Efficacy (cure rate) Secondary: Adverse events	Primary: A greater proportion of patients who received permethrin were lice-free two weeks following treatment with permethrin compared to lindane (98 vs 76%; *P*<0.001). Secondary: Mild dermal reactions, such as pruritus or erythema occurred in 1.2% of permethrin-treated patients and 2.6% of lindane-treated patients.
Kalter et al[38] Lindane shampoo 1% vs permethrin crème rinse 1%	RCT Men with the diagnosis of pediculosis pubis	N=53 10 days	Primary: Efficacy (cure rate) Secondary: Tolerability	Primary: There was no difference in the percentage of patients treated with lindane or permethrin who were cured at the final assessment (60 vs 57%; *P*>0.05). Secondary: Only one mild adverse reaction was reported in each group.
Carson et al[39] Permethrin crème rinse 1% vs	RCT Patients ≥4 years of age head lice	N=58 2 weeks	Primary: Efficacy (cure rate) Secondary: Tolerability	Primary: Permethrin was significantly more effective than the combination of pyrethrins and piperonyl butoxide at seven days following treatment with regard to cure rate (96.3 vs 45.2%; *P*<0.005). There was no statistically significant difference between the treatment

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
pyrethrins and piperonyl butoxide liquid				groups in subjects who were lice-free at day 14 (100 vs 93.5% in the permethrin and pyrethrins and piperonyl butoxide-treated subjects, respectively; *P*>0.01). Secondary: No adverse events were reported
DiNapoli et al[40] Permethrin crème rinse 1% vs pyrethrins combined with piperonyl butoxide	MC, R, SB Patients with pediculosis capitis (head lice infestation)	N=435 2 weeks	Primary: Efficacy (cure rate) Secondary: Adverse events	Primary: A total of 98% of the permethrin-treated patients and 85% of the pyrethrins and piperonyl butoxide-treated patients were free of lice at seven days. Prior to nit removal at 14 days, 96% of the permethrin-treated and 62% of the pyrethrins and piperonyl butoxide-treated patients remained lice-free. Secondary: Seventeen (7%) permethrin-treated and 32 (16%) pyrethrins and piperonyl butoxide-treated patients reported adverse events.
Roberts et al[41] Malathion lotion 0.5% vs wet combing with a fine-toothed comb	RCT Schoolchildren (aged 3 to 14 years) in Wales and the United Kingdom	N=81 2 weeks	Primary: Efficacy (cure rate) Secondary: Not reported	Primary: The cure rate was higher for patients treated with malathion compared to wet combing alone (78 vs 38%; *P* value not reported). Children assigned wet combing were 2.8 times more likely to have lice present at the end of treatment compared to the malathion group (95% CI, 1.5 to 5.2; *P*=0.0006). Secondary: Not reported
Chosidow et al[42] Malathion lotion 0.5% vs oral ivermectin in a single oral dose of 400 µg/kg	CR, CT, DB, DD, MC Patients ≥2 years of age with confirmed infestation and previously failed treatment with a pyrethroid-	N=812 15 days	Primary: Absence of head lice on day 15 Secondary: Absence of live head lice on days two and eight, as well as on days	Primary: On day 15, 95.2% of patients in the ivermectin ITT population were free of head lice compared to 85.0% of patients in the malathion group (difference, 10.2%; 95% CI, 4.6 to 15.7; *P*<0.001). On day 15, 97.1% of patients in the ivermectin per-protocol population were free of head lice compared to 89.8% of patients in the malathion group (difference, 7.3%; 95% CI, 2.8 to 11.8; *P*=0.002). Secondary:

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
	based or malathion insecticide two to six weeks before the first visit		22 and 29 for patients who entered the extension stage	A higher cure rate (absence of head lice) was achieved by day two in the ivermectin group compared to patients receiving malathion (92.4 vs 82.4%; *P*<0.001) and day eight (83.6 vs 53.9%; *P*<0.001). On day 15, eight patients in the ivermectin group and 31 in the malathion group had persistent infestation and entered the extension phase by switching to the other treatment. At day 29, all eight patients (100%) switched from ivermectin to malathion and 30 of the 31 patients (96.8%) switched from malathion to ivermectin lice-free (*P* values not reported).
Nofal et al[43] Malathion lotion 0.5% vs oral ivermectin in a single oral dose of 200 µg/kg	AC, RCT Children with head lice who were attending an outpatient clinic.	N=80 29 days	Primary: Presence of live lice and any side effects at day eight, 15 and 29 Secondary: Not reported	Primary: At day eight (after a single dose) there was a trend towards a higher cure rate in the malathion group compared to the ivermectin group, however, the difference was not statistically significant (87.5 vs 77.5%; *P*>0.05). The cure rate increased in both treatment groups after nonresponders were given a second dose (day 15), but the difference remained nonsignificant (95.0 vs 92.5% for malathion and ivermectin, respectively; *P*>0.05). By day 29, cure rates remained similar between the malathion and ivermectin treatment groups (80 vs 75%, respectively; *P*>0.05). Secondary: Not reported
Meinking et al[44] Malathion lotion 0.5% vs permethrin crème rinse 1%	Observer-blinded Patients with head lice	N=66 15 days	Primary: Efficacy (cure rate) Secondary: Not reported	Primary: At day 15, malathion was significantly more pediculicidal and ovicidal compared to permethrin (*P*<0.0001). Secondary: Not reported

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
Hipolito et al[45] Permethrin crème rinse 1% vs trimethoprim and sulfamethoxazole oral suspension 10 mg/kg/day vs permethrin crème rinse 1% plus trimethoprim and sulfamethoxazole oral suspension 10 mg/kg/day	MC, RCT Children aged 2 to 13 years	N=115 1 month	Primary: Efficacy (cure rate) Secondary: Adverse events	Primary: At the two-week follow-up, treatment success was reported in 79.5, 83.0 and 95.0% of patients who received permethrin, trimethoprim and sulfamethoxazole, and permethrin plus trimethoprim and sulfamethoxazole, respectively (*P* values not reported). At the four-week follow-up, successful treatment was reported for 72.0, 78.0 and 92.5% of those receiving permethrin, trimethoprim and sulfamethoxazole, and permethrin with trimethoprim and sulfamethoxazole groups, respectively (*P* values not reported). The absolute risk reduction for recurrence comparing permethrin to trimethoprim and sulfamethoxazole was 6%, trimethoprim and sulfamethoxazole to permethrin combined with trimethoprim and sulfamethoxazole was 14%, and permethrin vs permethrin combined with trimethoprim and sulfamethoxazole was 20% (*P*=0.03). Secondary: There were three trimethoprim and sulfamethoxazole-related rashes. Of the 115 participants, eight had minor adverse reactions to the treatment.
Meinking et al[46] Malathion 0.5% gel administered for 30, 60 or 90 minutes or malathion lotion 0.5% vs permethrin crème rinse 1%	AC, PG, RCT, investigator-blinded Patients with ≥3 live lice and 10 viable eggs	N=174 15 days	Primary: Efficacy (cure rate) Secondary: Safety results	Primary: At the end of the treatment period, malathion gel had a cure rate of 98, 93 and 86% when administered for 30, 60 or 90 minutes, respectively (*P*<0.05 for all time periods). Malathion lotion had a cure rate of 97% (*P*=0.0006). All groups were compared to permethrin which had a cure rate of 45%. Secondary: Adverse events were mild to moderate with erythema, headaches and nausea being the most common across all treatment groups.

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
Stough et al[47] Spinosad 0.9% topical suspension without nit combing vs permethrin 1% topical solution with nit combing vs spinosad 0.9% topical suspension with nit combing	2 AC, MC, PG, RCT, SB Healthy patients ≥6 months of age with head lice	N=1,038 14 days (up to 21 days for patients who received a second course of treatment)	Primary: Efficacy (cure rate) Secondary: Proportion of patients requiring one or two treatments	Primary: Treatment with spinosad without nit combing resulted in a significantly greater proportion of lice-free patients 14 days after treatment compared to permethrin with nit combining (*P*<0.001 for both trials). Results were similar when data from all of the patients (primary and nonprimary) were analyzed regardless of how many treatments were received. Both treatments were well tolerated, and no severe adverse events were reported. The most common adverse events were eye and scalp irritation. Overall, spinosad-treated patients had fewer adverse events; however, only application site erythema was significantly more frequent with permethrin-treated patients (*P*=0.007). Secondary: Overall, the majority of spinosad-treated patients (with or without nit combining) required only one treatment application for complete eradication of lice, whereas the majority of permethrin-treated patients required two treatments. In trial one, 94.2 and 68.1% of spinosad without nit combining- and permethrin with nit combing-treated patients required only one treatment (*P* value not reported). The corresponding numbers in trial two were 93.1 and 62.4%, respectively (*P* value not reported). After two treatments, 55.7 and 64.3% of spinosad without nit combing-treated patients were lice-free in both trials, compared to 33.3 and 27.1% of permethrin with nit combing-treated patients (*P* values not reported).

*Not available in the United States.
Study abbreviations: AC=active control, CI=confidence interval, CR=cluster randomized, CT=controlled trial, DB=double-blind, DD=double-dummy, ITT=intent-to-treat, MC=multicenter, OL= open-label, PG=parallel-group, PRO=prospective, R=randomized, RCT=randomized controlled trial, SB=single-blind

Special Populations

Table 5. Special Populations[7-14,16]

Generic Name	Population and Precaution				
	Elderly/ Children	Renal Dysfunction	Hepatic Dysfunction	Pregnancy Category	Excreted in Breast Milk
Single-Entity Agents					
Benzyl alcohol	Safety and efficacy in elderly patients have not been established. FDA-approved for use in children ≥6 months of age.	Not studied in renal dysfunction.	Not studied in hepatic dysfunction.	B	Unknown; caution is advised.
Crotamiton	Safety and efficacy in elderly patients have not been established. Not approved for use in pediatric populations.	Not studied in renal dysfunction.	Not studied in hepatic dysfunction.	C	Unknown: caution is advised.
Ivermectin	Safety and efficacy in elderly patients have not been established. FDA-approved for use in children ≥6 months of age.	Not studied in renal dysfunction.	Not studied in hepatic dysfunction.	C	Yes*
Lindane	Safety and efficacy in elderly patients have not been established. Should not be used in very young children or premature infants due to risk of seizures and death.	Not studied in renal dysfunction.	Not studied in hepatic dysfunction.	C	Enters breast milk; use is contra-indicated.
Malathion	Safety and efficacy in elderly patients	Not studied in renal dysfunction.	Not studied in hepatic dysfunction.	B	Unknown: risk cannot be ruled out;

Generic Name	Population and Precaution				
	Elderly/ Children	Renal Dysfunction	Hepatic Dysfunction	Pregnancy Category	Excreted in Breast Milk
	have not been established. FDA-approved for use in children ≥6 years of age.				caution is advised.
Permethrin	Safety and efficacy in elderly patients have not been established. FDA-approved for use in children ≥2 months of age.	Not studied in renal dysfunction.	Not studied in hepatic dysfunction.	B	Unknown: risk cannot be ruled out; caution is advised.
Spinosad	Safety and efficacy in elderly patients have not been established. FDA-approved for use in children ≥4 years of age.	Not studied in renal dysfunction.	Not studied in hepatic dysfunction.	B	No
Combination Products					
Piperonyl butoxide and pyrethrins	Safety and efficacy in elderly patients have not been established. FDA-approved for use in children ≥2 years of age.	Not studied in renal dysfunction.	Not studied in hepatic dysfunction.	Piperonyl butoxide- Unknown Pyrethrins- C	Unknown: risk cannot be ruled out; caution is advised.

* Following oral administration, ivermectin is excreted in human milk in low concentrations; this has not been evaluated following topical administration.

Adverse Drug Events

Table 6. Adverse Drug Events (%)[7-14,16]

Adverse Event(s)	Benzyl alcohol	Crotamiton	Ivermectin	Lindane	Malathion	Permethrin	Piperonyl Butoxide and Pyrethrins	Spinosad
Central Nervous System								
Ataxia	-	-	-	✔	-	-	-	-
Dizziness	-	-	-	✔	-	-	-	-
Fever	-	-	-	-	-	✔	-	-
Headache	-	-	-	✔	-	✔	-	-
Pain	-	-	-	✔	-	-	-	-
Seizures	-	-	-	✔	-	✔	-	-
Dermatological								
Alopecia	-	-	-	✔	-	-	-	0.1 to 1
Application site dryness/exfoliation	-	-	-	-	-	-	-	0.1 to 1
Dermatitis	-	✔	<1	✔	-	-	-	-
Dry skin	-	-	<1	-	-	-	-	0.1 to 1
Erythema	10	-	-	-	-	1 to 10	-	3
Itching	-	-	-	-	-	✔	-	-
Irritation of skin and scalp	-	✔	-	-	✔	-	✔	1
Mild transient burning/stinging	-	-	<1	✔	-	1 to 10	✔	-
Numbness	-	-	-	-	-	1 to 10	-	-
Pruritus	12	✔	-	✔	-	1 to 10	✔	-
Pyoderma	7	-	-	-	-	-	-	-
Rash	-	✔	-	-	-	1 to 10	-	-
Urticaria	-	-	-	✔	-	-	-	-
Gastrointestinal								
Abdominal pain	-	-	-	-	-	✔	-	-
Diarrhea	-	-	-	-	-	✔	-	-
Nausea	-	-	-	✔	-	✔	-	-
Vomiting	-	-	-	✔	-	✔	-	-
Other								
Aplastic anemia	-	-	-	✔	-	-	-	-

Adverse Event(s)	Benzyl alcohol	Crotamiton	Ivermectin	Lindane	Malathion	Permethrin	Piperonyl Butoxide and Pyrethrins	Spinosad
Cardiac arrhythmia	-	-	-	✔	-	-	-	-
Conjunctivitis (if eye contact)	-	-	<1	-	✔	-	-	-
Edema	-	-	-	-	-	1 to 10	-	-
Hematuria	-	-	-	✔	-	-	-	-
Hepatitis	-	-	-	✔	-	-	-	-
Ocular edema	-	-	-	-	-	-	-	2
Ocular irritation/hyperemia	6	-	<1	-	-	-	-	2
Paresthesia	-	-	-	✔	-	-	-	-
Pulmonary edema	-	-	-	✔	-	-	-	-

* Malathion is an insecticide/pesticide. Inadvertent transmucosal will manifest as excessive cholinergic activity (e.g., increased sweating, salivary and gastric secretion, gastric and uterine motility, and bradycardia). Additionally, malathion contains flammable alcohol and should not be exposed to an open flame or electric heat, including hair dryers and electric curlers.

✔ Frequency not specified (includes post marketing and case reports).

- Event not reported.

Contraindications/Precautions[7-14]

All topical scabicide and pediculicide products are contraindicated in patients with a sensitivity or allergy to any active or inactive ingredient in the product. [7-14]

For all topical scabicide and pediculicide products, eye exposure should be avoided, as these agents may cause eye irritation. If the product comes in contact with the eyes, flush eyes immediately with water; if irritation persists, consult a physician. [7-14,16]

Systemic exposure to benzyl alcohol has been associated with neonatal gasping syndrome consisting of severe metabolic acidosis, gasping respirations, progressive hypotension, seizures, central nervous system depression, intraventricular hemorrhage, and death in preterm, low birth weight infants. Neonates (i.e., patients less than one month of age or preterm infants with a corrected age of less than 44 weeks) could be at risk for gasping syndrome if treated with benzyl alcohol 5% or spinosad. [7,13]

Crotamiton should not be applied to acutely inflamed skin or raw or weeping surface until the acute inflammation has subsided.[8]

Lindane products should only be used in patients who cannot tolerate or have failed first-line treatment with safer medications for the treatment of head lice or scabies. Lindane can be poisonous if misused. If someone other than the patient will be applying lindane to the patient, they should wear less permeable gloves such as nitrile, latex with neoprene, or sheer vinyl, and thoroughly clean their hands after application. Natural latex gloves should be avoided because they are more permeable to lindane. If the person applying lindane could be pregnant, contact with lindane should be avoided. If the patient may be pregnant, other treatments may be preferable. The skin should be thoroughly cleaned prior to application, as oils can increase absorption, possibly increasing the risk of neurotoxicity. Wait at least one hour after bathing or showering before putting lindane on the skin due to increased permeability with wet or warm skin. Seizures and deaths have been reported following lindane use with repeat or prolonged application, but also in rare cases following a single application used according to directions. Lindane should be used with caution in infants, children, the elderly, and individuals with other skin conditions (e.g., atopic dermatitis, psoriasis) and in those who weigh less than 50 kilograms, as they may be at risk of serious neurotoxicity. Lindane is contraindicated in premature infants and individuals with known uncontrolled seizure disorders.[10]

Malathion lotion is contraindicated for neonates and infants because their scalps are more permeable and may have increased absorption of malathion. Malathion lotion is flammable**.** The lotion and wet hair should not be exposed to open flames or electric heat sources, including hair dryers and electric curlers. Do not smoke while applying lotion or while hair is wet. Allow hair to dry naturally and to remain uncovered after application of malathion lotion. Chemical burns including second-degree burns and stinging may occur when using malathion lotion.[11]

For patients allergic to ragweed, permethrin may cause breathing difficulty or an asthmatic episode while using permethrin-containing products.[12]

Black Box Warning for Lindane[10]

WARNING
Only use lindane in patients who cannot tolerate or have failed first-line treatment with safer medications for the treatment of scabies. Neurologic toxicity: Seizures and deaths have been reported following lindane use with repeat or prolonged application, but also in rare cases following a single application used according to directions. Exercise caution when using lindane in infants, children, the elderly and individuals with other skin conditions (e.g., atopic dermatitis, psoriasis) and in those who weigh less than 110 lbs (50 kg) as they may be at risk of serious neurotoxicity.

WARNING
Contraindications: Lindane is contraindicated in premature infants and individuals with known uncontrolled seizure disorders. Proper use: Instruct patients on the proper use of lindane, the amount to apply, how long to leave it on, and avoiding retreatment. Inform patients that itching occurs after the successful killing of scabies and is not necessarily an indication for retreatment with lindane.

Drug Interactions

There are no significant drug interactions with the scabicides and pediculicides.[7-14] Lindane should be used with caution with any drug that is known to lower the seizure threshold. These include antipsychotics, antidepressants, theophylline, cyclosporine, mycophenolate, tacrolimus, penicillins, imipenem, fluoroquinolones, chloroquine, isoniazid, meperidine, radiographic contrast media, centrally active anticholinesterases, and methocarbamol.[10]

Dosage and Administration

Table 7. Dosing and Administration[7-14]

Generic Name	Adult Dose	Pediatric Dose	Availability
Single-Entity Agents			
Benzyl alcohol	Head lice: Lotion: apply sufficient lotion to dry hair to completely saturate the scalp; leave for 10 minutes, then rinse off with water; repeat treatment after seven days	Head lice: Lotion: apply sufficient lotion to dry hair to completely saturate the scalp; leave for 10 minutes, then rinse off with water; repeat treatment after seven days	Lotion: 5% (227 g/bottle)
Crotamiton	Scabies: Cream, lotion: prior to application, patients should bathe or shower. A thin layer of cream or lotion should be thoroughly massaged into all skin surfaces from the chin down to the toes including all skin folds and creases. Crotamiton is left on the skin and a second application is advisable 24 hours later. The patient should take a cleansing bath 24 to 48 hours after the last application to remove any remaining drug. Patients can be retreated after seven days if live mites appear or if no clinical improvement is observed	Scabies: Cream, lotion: prior to application, patients should bathe or shower. A thin layer of the cream or lotion should be thoroughly massaged into all skin surfaces from the chin down to the toes including all skin folds and creases. Crotamiton is left on the skin and a second application is advisable 24 hours later. The patient should take a cleansing bath 24 to 48 hours after the last application to remove any remaining drug. Patients can be retreated after seven days if live mites appear or if no clinical improvement is observed Due to potential lindane toxicity, crotamiton is a drug of choice for young children	Cream: 10% (2 oz/ tube) Lotion: 10% (2 oz/bottle, 16 oz/bottle)

Generic Name	Adult Dose	Pediatric Dose	Availability
		and pregnant or lactating women in the treatment of scabies. However, crotamiton is not approved by the Food and Drug Administration (FDA) for the treatment of scabies in pediatric patients.	
Ivermectin	Head lice: Lotion: apply to dry hair in an amount sufficient (up to one tube) to thoroughly coat the hair and scalp. Leave lotion in place for 10 minutes and then rinse off with water.	Head lice: Lotion: apply to dry hair in an amount sufficient (up to one tube) to thoroughly coat the hair and scalp. Leave lotion in place for 10 minutes and then rinse off with water. This should be used in children six months or older.	Lotion: 0.5% (4 oz/tube)
Lindane	Head and pubic lice: Shampoo: apply a sufficient quantity of shampoo onto clean, dry hair; generally one ounce is sufficient, no more than two ounces should be used. Work the shampoo into hair thoroughly and allow remaining on hair for four minutes. Add small quantities of water and massage until a good lather forms. Rinse thoroughly and towel dry briskly. Nits should be removed using a nit comb or tweezers. Retreatment is not recommended Scabies: Lotion: one ounce of lindane is generally sufficient to treat the average adult. Do not use more than two ounces for larger adults. The lotion should be applied thinly and rubbed in thoroughly. Avoid applying lindane to open cuts. The lotion should be left on for 8 to 12 hours and removed by thorough washing. Retreatment is not recommended	The use of lindane should be avoided in infants and young children due to a higher incidence of adverse reactions in this age group.	Lotion: 1% (2 oz/bottle) Shampoo: 1% (2 oz/bottle)
Malathion	Head lice: Lotion: apply to dry hair in an amount sufficient to	Head lice: Lotion: apply to dry hair in an amount sufficient to	Lotion: 0.5% (2 oz/ bottle)

Generic Name	Adult Dose	Pediatric Dose	Availability
	thoroughly wet the hair and scalp. Allow hair to dry naturally, do not use an electric heat source, and allow hair to remain uncovered. After 8 to 12 hours, the hair should be shampooed. Rinse and use a fine-toothed (nit) comb to remove dead lice and eggs. If lice are still present after seven to nine days, repeat with a second application of lotion	thoroughly wet the hair and scalp. Allow hair to dry naturally, do not use an electric heat source, and allow hair to remain uncovered. After 8 to 12 hours, the hair should be shampooed. Rinse and use a fine-toothed (nit) comb to remove dead lice and eggs. If lice are still present after seven to nine days, repeat with a second application of lotion This should be used in children six months or older.	
Permethrin	Head lice: Cream, lotion: a sufficient volume (25 to 50 mL) applied to saturate the hair and scalp. A second application may be indicated if live lice are present seven days or more after the initial application Scabies: Cream: 30 g is usually sufficient for an average adult to provide for a single head to toe application. Repeat dose 14 days later if living mites are observed	Head lice: Cream, lotion: a sufficient volume (25 to 50 mL) applied to saturate the hair and scalp. A second application may be indicated if live lice are present seven days or more after the initial application Scabies: Cream: 30 g is usually sufficient for an average adult to provide for a single head to toe application. Repeat dose 14 days later if living mites are observed This should be used in children two months or older.	Cream: 5% (2 oz/tube) Liquid: 1% (2 oz/bottle) Lotion: 1% (2 oz/bottle, 4 oz/bottle)
Spinosad	Head lice: Suspension: apply sufficient amount to cover dry scalp, then apply to dry hair. Depending on hair length, apply up to 120 mL (one bottle) to adequately cover scalp and hair. Leave on for 10 minutes, and then thoroughly rinse off with warm water. If live lice are seen seven days following the first treatment, a second treatment should be applied	Head lice: Suspension: apply sufficient amount to cover dry scalp, then apply to dry hair. Depending on hair length, apply up to 120 mL (one bottle) to adequately cover scalp and hair. Leave on for 10 minutes, and then thoroughly rinse off with warm water. If live lice are seen seven days following the first treatment, a second treatment should be applied This should be used in	Topical Suspension: 0.9% (4 oz/bottle)

Generic Name	Adult Dose	Pediatric Dose	Availability
		children four years of age or older.	
Combination Products			
Piperonyl butoxide and pyrethrins	Head, body and pubic lice: Solution: the undiluted liquid should be applied to dry hair and scalp or to any infested area until entirely wet. The liquid should not be used on the eyelashes or eyebrows Shampoo: apply to the affected area until all hair is thoroughly wet and allowed to stand for no longer than 10 minutes. Then, the area should be washed with warm water and shampoo or soap. A fine-toothed comb, usually supplied with the product, should be used to remove dead lice and ova. The treatment should be repeated in 7 to 10 days to assure eradication of unhatched nits. Two consecutive applications should not be administered within 24 hours	Head, body and pubic lice: Solution: the undiluted liquid should be applied to dry hair and scalp or to any infested area until entirely wet. The liquid should not be used on the eyelashes or eyebrows Shampoo: apply to the affected area until all hair is thoroughly wet and allowed to stand for no longer than 10 minutes. Then, the area should be washed with warm water and shampoo or soap. A fine-toothed comb, usually supplied with the product, should be used to remove dead lice and ova. The treatment should be repeated in 7 to 10 days to assure eradication of unhatched nits. Two consecutive applications should not be administered within 24 hours This should be used in children two years of age or older.	Gel: 4/0.33% (each kit) Shampoo: 4/0.33% (each kit) Solution: 4/0.33% (each kit)

Clinical Guidelines

Table 8. Clinical Guidelines

Clinical Guideline	Recommendations
Centers for Disease Control and Prevention: **Treatment of Head Lice (2010)**[19]	• Treatment for head lice is recommended for persons diagnosed with an active infestation. All household members and other close contacts should be checked; those persons with evidence of an active infestation should be treated. • Some experts believe prophylactic treatment is prudent for persons who share the same bed with actively-infested individuals. All infested persons (household members and close contacts) and their bedmates should be treated at the same time. • Retreatment of head lice usually is recommended because no approved pediculicide is completely ovicidal. To be most effective, retreatment should occur after all eggs have hatched and before new eggs are produced. The retreatment schedule can vary depending on whether the pediculicide used is ovicidal. • When treating head lice, non-pharmacologic measures can be combined with

Clinical Guideline	Recommendations
	recommended medicine; however, such measures generally are not required to eliminate a head lice infestation. Over-the-counter medications • Pyrethrin or permethrin-containing products are approved by the Food and Drug Administration (FDA) for the treatment of head lice and are available over-the-counter. • Pyrethrins only kill live lice, not unhatched eggs (nits). A second treatment is recommended on day nine to kill newly hatched lice before they produce new eggs. • Permethrin is a synthetic pyrethroid similar to naturally occurring pyrethrins. Permethrin kills live lice but not unhatched eggs. Permethrin may continue to kill newly hatched lice for several days after treatment. A second treatment often is necessary on day nine to kill newly hatched lice before they produce new eggs. Prescription medications • Malathion is pediculicidal and partially ovicidal. A second treatment is recommended if live lice still are present seven to nine days after treatment. • Benzyl alcohol lotion 5% kills live lice but does not kill unhatched lice eggs. A second treatment is required nine days after the first treatment to kill any newly hatched lice before they can produce new eggs. • Lindane is an organochloride. The American Academy of Pediatrics no longer recommends using this agent for the treatment of lice. Incorrect use of lindane can be neurotoxic; its use should be restricted to patients for whom prior treatments have failed or who cannot tolerate safer medications. Lindane should not be used to treat premature infants, persons with human immunodeficiency virus, a seizure disorder, women who are pregnant or breast-feeding, persons who have very irritated skin or sores where the lindane will be applied, infants, children, the elderly, and persons who weigh less than 110 pounds.
American Academy of Pediatrics: **Clinical Report-Head Lice (2010)**[20]	Treatment • Therapy could be initiated with permethrin 1% or pyrethrins when resistance to these products is not suspected. These agents are available over-the-counter without a prescription. • Malathion 0.5% can be used in people who are ≥24 months of age when resistance to permethrin or pyrethrins is documented or when treatment with these products fails despite their correct use. • Other treatments can be considered for people who cannot afford or who wish to avoid pediculicides. Improper application of the pediculicide should be considered first as a cause of treatment failure. • Permethrin is the most studied pediculicide in the United States (U.S.) and is the least toxic to humans. Permethrin is less allergenic than pyrethrins and does not cause allergic reactions in individuals with plant allergies. Permethrin leaves a residue on the hair that kills nymphs emerging from the 20 to 30% of eggs not killed by the first application. However, conditioners and silicone-based additives present in almost all currently available shampoos impair permethrin adherence to the hair shaft and reduce its residual effect. Application should be repeated in seven to 10 days if live lice are seen. Many experts now recommend routine retreatment, preferably on day nine. An alternate treatment schedule on days zero, seven, and 13 to 15 has been proposed for nonovicidal products.

Clinical Guideline	Recommendations
	• Resistance to 1% permethrin has been reported, but the prevalence of this resistance is not known. • Pyrethrins are formulated with piperonyl butoxide. Pyrethrins are neurotoxic to lice but have extremely low mammalian toxicity. Pyrethrins are applied to dry hair and left on for 10 minutes before rinsing out. No residual pediculicidal activity remains after rinsing. In addition, none of these natural pyrethrins are totally ovicidal and 20 to 30% of the eggs remain viable after treatment, requiring a second treatment. New evidence based on the life cycle of lice suggests that retreatment at day nine is optimal. An alternate schedule of three treatments with nonovicidal products on days zero, seven, and 13 to 15 has been proposed. • Malathion is a prescription lotion that is applied to dry hair, left to air dry, then washed off after eight to 12 hours. The current U.S formulation of malathion differs from the malathion products available in Europe in that it contains terpineol, dipentene, and pine needle oil, which themselves have pediculicidal properties and may delay development of resistance. Malathion has high ovicidal activity, and a single application is adequate for most patients. The product should be reapplied in seven to nine days if live lice are still seen. Due to the high alcohol concentration of the product it is highly flammable. • Benzyl alcohol 5% is kills head lice by asphyxiation. Benzyl alcohol is available by prescription and is not ovicidal. It should be applied topically for 10 minutes and repeated in seven days, although as with other nonovicidal products, consideration should be given to retreating in nine days or using three treatment cycles. • Lindane is an organochloride that has central nervous system toxicity in humans. It has low ovicidal activity (30 to 50% of eggs are not killed), and resistance has been reported worldwide for many years. For these reasons, it should be used cautiously. The FDA has warned that lindane shampoo should only be used for patients who cannot tolerate or whose infestation has failed to respond to first-line treatment with safer medications for the treatment of head lice.
Center for Disease Control and Prevention Morbidity and Mortality Weekly Report: **Sexually Transmitted Diseases Treatment Guidelines (2010)**[48]	Pediculosis pubis (pubic lice infestation) • Recommended regimens include permethrin 1% cream rinse applied to affected areas and washed off after 10 minutes or piperonyl butoxide and pyrethrins applied to the affected area and washed off after 10 minutes. • Alternative regimens include malathion 0.5% lotion applied for eight to 12 hours and washed off or ivermectin 250 µg/kg orally repeated in two weeks. Scabies • Recommended regimens include permethrin 5% cream applied to all areas of the body from the neck down and washed off after eight to 14 hours or ivermectin 200 µg/kg orally, repeated in two weeks. • Alternative regimens include lindane 1% lotion (one ounce) or cream (30 g) applied in a thin layer to all areas of the body from the neck down and thoroughly washed off after eight hours.
Centers for Disease Control and Prevention: **Treatment of Scabies (2010)**[49]	Suggested general guidelines • Lotion or cream should be applied to all areas of the body from the neck down to the feet and toes. When treating infants and young children, scabicide lotion or cream also should be applied to their entire head and neck because scabies can affect their face, scalp, and neck, as well as the rest of their body. The lotion or cream should be applied to a clean body and left on for the recommended time before washing it off. Clean clothing should

Clinical Guideline	Recommendations
	be worn after treatment. Medications • Permethrin is the drug of choice for the treatment of scabies and is approved in persons at least two months of age. Permethrin kills scabies mite and eggs. Two (or more) applications may be necessary to eliminate all mites, particularly when treating crusted (Norwegian) scabies. • Crotamiton is approved for the treatment of scabies in adults. Crotamiton is not approved for use in children. This agent is frequently associated with treatment failure. • Lindane is not recommended as a first-line therapy. Incorrect use of lindane can be toxic to the brain and other parts of the nervous system; its use should be restricted to patients who have failed recommended therapies or who cannot tolerate recommended treatments. • Lindane should not be used to treat premature infants, persons with a seizure disorder, women who are pregnant or breast-feeding, persons who have very irritated skin or sores where the lindane will be applied, infants, children, the elderly, and persons who weigh less than 110 pounds. • Ivermectin is an oral antiparasitic agent approved for the treatment of worm infestations. Oral ivermectin may be safe and effective for the treatment of scabies; however, ivermectin is not approved for this use. Oral ivermectin has been reported effective in the treatment of crusted scabies; its use should be considered for patients who have failed treatment with or who cannot tolerate topical medications for the treatment of scabies. • The dosage of ivermectin is 200 µg/kg orally. Two or more doses at least seven days apart may be necessary to eliminate a scabies infestation. The safety of ivermectin in children weighing less than 15 kg and in pregnant women has not been established.
Centers for Disease Control and Prevention: **Treatment of Pubic Lice (2010)**[50]	Medications • A lice-killing lotion containing 1% permethrin or a mousse containing pyrethrins and piperonyl butoxide can be used to treat pubic lice. These products are available over-the-counter without a prescription. • Lindane shampoo is a prescription medication that can kill lice and lice eggs. However, lindane is not recommended as a first-line therapy. Lindane can be toxic to the brain and other parts of the nervous system; its use should be restricted to patients who have failed treatment with or cannot tolerate recommended therapies. Lindane should not be used to treat premature infants, persons with a seizure disorder, women who are pregnant or breast-feeding, persons who have very irritated skin or sores where the lindane will be applied, infants, children, the elderly, and persons who weigh less than 110 pounds. • Malathion lotion is a prescription medication that can kill lice and some lice eggs but has not been approved by the FDA for this indication. • Ivermectin has been used successfully to treat lice; but only has not been approved by FDA for treatment of lice. Of note, in 2012, a topical formulation of ivermectin was approved for the treatment of head lice infestations.

Conclusions

There are a number of effective topical scabicide and pediculicide agents available including benzyl alcohol (Ulesfia®), crotamiton (Eurax®), ivermectin (Sklice®), lindane, malathion (Ovide®), permethrin (Nix®), piperonyl butoxide with pyrethrins (RID®) and spinosad (Natroba®).[7-14] Permethrin products are recommended as first-line therapy for treatment of scabies and lice, despite increasing resistance in the

United States.[18-20] The topical insecticides exert their pediculicidal and scabicidal effects through their neurotoxic actions on lice. Benzyl alcohol acts via asphyxiation of the parasite rather than neuroexcitation, theoretically lowering the risk of resistance.[7] Ivermectin and spinosad are two newer agents approved for the treatment of head lice. Spinosad is not extensively metabolized, and therefore it is still present, and able to exert its effect when the lice eggs hatch and the nervous system develops. This may prevent the need for a second administration if no live lice are observed several days following the initial application.[6] Ivermectin has been approved for one-time use.[13] The permethrin products reviewed here, as well as their generic equivalents, are available over-the-counter (OTC).[16] Lindane is reserved as second-line therapy and carries a Black Box Warning describing risk of neurotoxicity associated with its use. Other available agents offer alternative options should a resistant case occur, or if a patient experiences treatment failure with an OTC product.[19-20]

A comparison of the overall success rates for the topical scabicide products shows 89 to 100% success with permethrin, 65 to 92% with lindane, and 60 to 88% with crotamiton. Permethrin is recommended as first-line therapy and lindane as second-line in the guidelines by the Centers for Disease Control (CDC) and the American Academy of Pediatrics.[19-20] Crotamiton also has a role as an antipruritic for those with scabies. [19] All patients treated for scabies should expect the rash and itching to continue for approximately two weeks after treatment.[2]

Overall, the comparative success rates of topical pediculicides have been shown to be approximately 57 to 99% with permethrin, 45 to 95% with piperonyl butoxide and pyrethrins, 60 to 88% with lindane and 78% with malathion. The newer agents which include benzyl alcohol, ivermectin and spinosad, have shown cure rates of 75%, 71 to 75% and 93 to 94%, respectively, although there is limited published literature confirming these results.[9,47] The CDC recommends permethrin or the combination of piperonyl butoxide and pyrethrins as equivalent therapies for pediculosis pubis.[50]

References

1. Roos TC, Alam M, Roos S, Merk HF, Bickers DR. Pharmacotherapy of ectoparasitic infections. Drugs. 2001;61:1067-88.
2. Wendel K, Rompalo A. Scabies and pediculosis pubis: an update of treatment regimens and general review. Clin Infect Dis. 2002;35(Suppl 2):S146-51.
3. Feldmeier H. Pediculosis capitis: new insights into epidemiology, diagnosis and treatment. Eur J Clin Microbiol Infect Dis. 2012 Sep;31(9):2105-10.
4. Chosidow O. Clinical practices. Scabies. N Engl J Med 2006; 354:1718.
5. Downs AMR, Harvey I, Kennedy CTC. The epidemiology of head lice and scabies in the UK. Epidemiol Infect 1999;122:471-477.
6. Villegas SC, Breitzka RL. Head lice and the use of spinosad. Clin Ther. 2012 Jan;34(1):14-23.
7. Ulesfia® [package insert]. Atlanta (GA): Shionogi Pharma Inc.; 2012 Jul.
8. Eurax® [package insert]. Jacksonville (FL): Ranbaxy; 2009 Jul.
9. Sklice® [package insert]. Swiftwater (PA): Sanofi Pasteur Inc.; 2012 Feb.
10. Lindane® [package insert]. Morton Grove (IL): Morton Grove Pharmaceuticals Inc.; 2005 Jun.
11. Ovide® [package insert]. Hawthome (NY): Taro Phrmaceuticals U.S.A., Inc.; 2011 Nov.
12. Permethrin: drug information. In: Rose BD, ed. UpToDate [database on the Internet]. Waltham, MA: UpToDate; 2013. [cited 2013 Jun 13]. Available from: http://www.uptodate.com/contents/permethrin-drug-information?source=search_result&search=Nix&selectedTitle=1%7E150
13. Natroba® [package insert]. Carmel (IN): ParaPro LLC.; 2011 May.
14. Pyrethrins: drug information. In: Rose BD, ed. UpToDate [database on the Internet]. Waltham, MA: UpToDate; 2013. [cited 2013 Jun 13]. Available from: http://www.uptodate.com/contents/pyrethrins-drug-information?source=search_result&search=pyrethrin&selectedTitle=1%7E11.
15. Spinosad (Natroba) topical suspension for head lice. Med Lett Drugs Ther. 2011 Jun 27;53(1367):50-1.
16. Drug Facts and Comparisons 4.0 [database on the Internet]. St. Louis: Wolters Kluwer Health, Inc.; 2013 [cited 2013 Jun 13]. Available from: http://online.factsandcomparisons.com.
17. Pollack RJ, Kiszewski A, Armstrong P, Hahn C, Wolfe N, Rahman HA, et al. Differential permethrin susceptibility of head lice sampled in the United States and Borneo. Arch Pediatr Adolesc Med. 1999;153:969-73.
18. Downs AM, Stafford KA, Harvey I, Coles GC. Evidence for double resistance to permethrin and malathion in head lice. Br J Dermatol. Sep 1999;141(3):508-11.
19. Treatment of Head Lice. Centers for Disease Control and Prevention. 2010. [cited 2013 Jun 13]. Available at: http://www.cdc.gov/lice/head/treatment.html.
20. Frankowski BL, Bocchini JA Jr; Council on School Health and Committee on Infectious Diseases. Head lice. Pediatrics. 2010 Aug;126(2):392-403. [cited 2013 Jun 13]. Available at: http://pediatrics.aappublications.org/content/early/2010/07/26/peds.2010-1308.
21. Micromedex® Healthcare Series [database on the Internet]. Greenwood Village (CO): Thomson Reuters (Healthcare) Inc.; Updated periodically [cited 2013 Jun 13]. Available from: http://www.thomsonhc.com/.
22. Haustein UF, Hlawa B. Treatment of scabies with permethrin vs lindane and benzyl benzoate. Acta Derm Venereol. 1989;69:348-51.
23. Schultz MW, Gomez M, Hansen RC, Mills J, Menter A, Rodgers H, et al. Comparative study of 5% permethrin cream and 1% lindane lotion for the treatment of scabies. Arch Dermatol. 1990;126:167-70.
24. Zargari O, Golchai J, Sobhani A, Dehpour AR, Sadr-Ashkevari S, Alizadeh N, et al. Comparison of the efficacy of topical 1% lindane vs. 5% permethrin in scabies: A randomized, double-blind study. Indian J Dermatol Venereol Leprol. 2006;72;33-6.
25. Taplin D, Meinking TL, Porcelain SL, Castilero PM, Chen JA. Permethrin 5% dermal cream: a new treatment for scabies. J Am Acad Dermatol. 1986;15:995-1001.
26. Taplin D, Meinking TL, Chen JA., Sanchez R. Comparison of crotamiton 10% cream (Eurax) and permethrin 5% cream (Elimite) for the treatment of scabies in children. Pediatr Dermatol. 1990;7:67-73.
27. Amer M, el-Garib I. Permethrin vs crotamiton and lindane in the treatment of scabies. Int J Dermatol.

1992;31:357-8.
28. Chouela EN, Abeldaño AM, Pellerano G, La Forgia M, Papale RM, Garsd A, et al. Equivalent therapeutic efficacy and safety of ivermectin and lindane in the treatment of human scabies. Arch Dermatol. 1999;135:651-5.
29. Madan V, Jaskiran K, Gupta U, Gupta DK. Oral ivermectin in scabies patients: a comparison with 1% topical lindane lotion. J Dermatol. 2001;28:481-4.
30. Usha V, Gopalakrishnan Nair TV. A comparative study of oral ivermectin and topical permethrin cream in the treatment of scabies. J Am Acad Dermatol. 2000; 42(2 Pt 1):236-40.
31. Goldust M, Rezaee E, Hemayat S. Treatment of scabies: Comparison of permethrin 5% vs ivermectin. Dermatol. 2012 Jun;39(6):545-7.
32. Chhaiya SB, Patel VJ, Dave JN, Mehta DS, Shah HA. Comparative efficacy and safety of topical permethrin, topical ivermectin, and oral ivermectin in patients of uncomplicated scabies. Indian J Dermatol Venereol Leprol. 2012 Sep;78(5):605-10.
33. Meinking TL, Villar ME, Vicaria M, Eyerdam DH, Paquet D, Mertz-Rivera K, et al. The clinical trials supporting benzyl alcohol lotion 5% (Ulesfia): a safe and effective topical treatment for head lice (pediculosis humanus capitis). Pediatr Dermatol. 2010 Jan-Feb;27(1):19-24.
34. Pariser DM, Meinking TL, Bell M, Ryan WG. Topical 0.5% ivermectin lotion for treatment of head lice. N Engl J Med. 2012 Nov;367(18):1687-93.
35. Brandenburg K, Deinard AS, DiNapoli J, Englender SJ, Orthoefer J, Wagner D.1% permethrin cream rinse vs. 1% lindane shampoo in treating pediculosis capitis. Am J Dis Child. 1986; 140:894-6.
36. Taplin D, Meinking TL, Castillero PM, Sanchez R. Permethrin 1% creme rinse for the treatment of Pediculus humanus var capitis infestation. Pediatr Dermatol. 1986;3:344-8.
37. Bowerman JG, Gomez MP, Austin RD, Wold DE. Comparative study of permethrin 1% creme rinse and lindane shampoo for the treatment of head lice. Pediatr Infect Dis J. 1987;6:252-5.
38. Kalter DC, Sperber J, Rosen T, Matarasso S. Treatment of pediculosis pubis. Clinical comparison of efficacy and tolerance of 1% lindane shampoo vs. 1% permethrin creme rinse. Arch Dermatol. 1987;123:1315-9.
39. Carson DS, Tribble PW, Weart CW. Pyrethrins combined with piperonyl butoxide (RID) vs. 1% permethrin (NIX) in the treatment of head lice. Am J Dis Child. 1988;142:768-9.
40. DiNapoli JB, Austin RD, Englender SJ, Gomez MP, Barrett JF. Eradication of head lice with a single treatment. Am J Public Health. 1988;78:978-80.
41. Roberts RJ, Casey D, Morgan DA, Petrovic M. Comparison of wet combing with malathion for treatment of head lice in the UK: a pragmatic randomized controlled trial. Lancet. 2000;356:540-4.
42. Chosidow O, Giraudeau B, Cottrell J, Izri A, Hofmann R, Mann SG, et al. Oral ivermectin vs malathion lotion for difficult-to-treat head lice. N Engl J Med. 2010 Mar 11;362(10):896-905.
43. Nofal A. Oral ivermectin for head lice: a comparison with 0.5 % topical malathion lotion. J Dtsch Dermatol Ges. 2010 Dec;8(12):985-8.
44. Meinking TL, Vicaria M, Eyerdam DH, Villar ME, Reyna S, Suarez G. Efficacy of a reduced application time of Ovide lotion (malathion) compared to nix crème rinse (1% permethrin) for the treatment of head lice. Pediatric Dermatology. 2004; 21(6);670-4.
45. Hipolito RB, Mallorca FG, Zuniga-Macaraig ZO, Apolinario PC, Wheeler-Sherman J. Head lice infestation: single drug vs combination therapy with one percent permethrin and trimethoprim/sulfamethoxazole. Pediatrics. 2001;107:E30.
46. Meinking TL, Vicaria M, Eyerdam DH, Villar ME, Reyna S, Suarez G. A Randomized, Investigator-Blinded, Time-Ranging Study of the Comparative Efficacy of 0.5% Malathion Gel Vs Ovide® Lotion (0.5% Malathion) or Nix® Crème Rinse (1% Permethrin) Used as Labeled, for the Treatment of Head Lice. Pediatric Dermatology. 2007; 24(4):405-11.
47. Stough D, Shellabarger MS, Quiring J, Gabrielsen AA. Efficacy and safety and spinosad and permethrin crème rinses for pediculosis capitis (head lice). Pediatrics. 2009;124:389e-95e.
48. Centers for Disease Control and Prevention. Ectoparasitic infections. In: Centers for Disease Control and Prevention. Sexually Transmitted Diseases Treatment Guidelines, 2010. MMWR 2010;59 (No. RR-12):1-110. [cited 2013 Jun 13]. Available at: http://www.cdc.gov/std/treatment/2010/ectoparasitic.htm

49. Treatment of Scabies. Centers for Disease Control and Prevention. 2010. [cited 2013 Jun 13]. Available at: http://www.cdc.gov/parasites/scabies/treatment.html.
50. Treatment of Pubic “Crab” Lice. Centers for Disease Control and Prevention. 2010. [cited 2013 Jun 13]. Available at: http://www.cdc.gov/parasites/lice/pubic/treatment.html.