

Therapeutic Class Overview Scabicides and Pediculicides

INTRODUCTION

- 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 pruritic eruption and itching. Pediculi or lice can cause infestations either on the head (*Pediculus humanus capitis*), body (*Pediculus humanus corporis*), or the pubic region (*Pthirus pubis*). These skin conditions are common causes of skin rash and pruritus (*Roos et al 2001, Wendel et al 2002*). Head lice infestation crosses all social and geographic boundaries and generally affects children, primarily females, aged three to 12 years (*Feldmeier 2012*). 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 (*Chosidow 2006, Downs et al 1999*). 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 (*Villegas et al 2012*).
- The topical agents indicated for the management of scabies and head lice are listed in Table 1. All of the agents included in this review are Food and Drug Administration (FDA)-approved for the treatment of head lice with the exception of Eurax (crotamiton), which is only indicated to treat scabies. Lindane lotion indicated to treat scabies has been discontinued; the shampoo is still available for the treatment of lice.
- The pediculicidal effects of most of these agents result from their neurotoxic effects on lice. These agents, except benzyl alcohol, cause periods of central nervous system hyperexcitation, resulting in paralysis and ultimately death of the lice. Ulesfia (benzyl alcohol) is unique in that it disables the breathing structure of the lice, resulting in asphyxiation rather than neuroexcitation. 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.
- RID (piperonyl butoxide, pyrethrum extract) and NIX (permethrin) are pediculicidal, but not ovicidal, and therefore require nit combing and retreatment in 7 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 8 to 12 hours of application and is highly flammable. Lindane is neurotoxic and is not recommended as an initial treatment option. Sklice (ivermectin) and Natroba (spinosad) are pediculicidal but not ovicidal. Topical ivermectin is approved as a single application product only.
- Some data suggest a growing resistance to permethrin in the United States, with recent studies stating that the effectiveness of permethrin has declined to 25% and resistance to pyrethrins is widespread (*Koch et al 2016, The Medical Letter 2016*). However, both the United States Centers for Disease Control and Prevention (CDC) as well as the American Academy of Pediatrics (AAP) continue to recommend permethrin as first-line therapy for treatment of both lice and scabies. Permethrin 1% or pyrethrins should be used when resistance is not suspected. Malathion (in patients who are 6 years of age or older) and benzyl alcohol (in children older than 6 months) are available as alternative agents if the first-line medications are inappropriate or ineffective. Spinosad and ivermectin might prove helpful in difficult cases, but are more costly. Lindane is no longer recommended for use as treatment of head lice (*AAP Red Book 2018, CDC 2015[a], CDC 2016, CDC 2018, Devore et al 2015, Downs et al 1999*).
- Medispan class: Scabicides and pediculicides and scabicide combinations.

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Table 1. Medications Included Within Class Review

Drug	Generic Availability
Eurax (crotamiton cream and lotion)	<mark>✓ ‡</mark>
Lindane (gamma-hexachlorocyclohexane)*	✓ ✓
Natroba (spinosad)	✓
Ovide (malathion)	✓
Permethrin (Elimite 5%, NIX 1% lice treatment [†])	✓
Piperonyl butoxide and pyrethrins (RID [†])	✓
Sklice (ivermectin)**	-
Ulesfia (benzyl alcohol)	-

†Over-the-counter (OTC) product is available in at least one dosage form or strength. Not all product options are listed as there are a number of OTC products available.

‡Generic Crotan (crotamiton lotion) is available; the cream is brand only.

*Lindane shampoo is available; the lotion formulation has been discontinued.

**Another product, trade name Soolantra, is available as a 1% cream and is indicated for rosacea.

(Drugs @FDA 2019, Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations 2019)

INDICATIONS

Table 2. Food and Drug Administration Approved Indications

Indication	Eurax (crotamiton)	Lindane (gamma- hexachlorocyclo hexane)	Natroba (spinosad)	Ovide (malathion)	Permethrin (Elimite, NIX)	Piperonyl butoxide and pyrethrins (RID)	Sklice (ivermectin)	Ulesfia (benzyl alcohol)
Scabies	~				✔ §#			
Head lice		✓ *	∨ ‡	√ †	✔ ∥#	✓ ¶	√ ‡	✓ ‡
Pubic (crab) lice		✓ *				✓ ¶		
Body lice						✓ ¶		

*Lindane shampoo is reserved for patients who cannot tolerate or have failed first-line treatment with safer medications for the treatment of head or pubic lice

+ In patients \geq 6 years of age

 \ddagger In patients \ge 6 months of age

§ Permethrin 5% cream is indicated for the treatment of scabies.

Permethrin 1% lotion/cream rinse is indicated for the treatment of head lice.

In patients ≥ 2 months of age

¶ In patients \geq 2 years of age

(Clinical Pharmacology 2019; Prescribing information: Elimite 2015, Eurax 2012, Lindane 2009, Natroba 2014, Ovide 2017, Sklice 2017, Ulesfia 2015)

 Information on indications, mechanism of action, pharmacokinetics, dosing, and safety has been obtained from the prescribing information for the individual products, except where noted otherwise.

CLINICAL EFFICACY SUMMARY

Scabies

Data as of Feb 1, 2019 RS-U/RR-U/AVD

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- 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 (*Amer et al 1992, Haustein et al 1989, Schultz et al 1990, Taplin et al 1986b, Taplin et al 1990, Zargari et al 2006*). In the largest study (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 (*Schultz et al 1990*). In a single-blind, randomized controlled trial comparing ivermectin to crotamiton (N = 340), 2 applications of ivermectin were as effective as a single application of crotamiton cream for the treatment of scabies at 2 weeks. After repeating therapy, ivermectin was superior to crotamiton cream at 4 weeks follow-up (*Goldust et al 2014*).
- Both Lindane and permethrin have also been compared to oral ivermectin for the treatment of scabies. Numerous studies have demonstrated a significantly lower cure rate after 4 weeks with Lindane compared to oral ivermectin (*Goldust et al 2013, Madan et al 2001, Mohebbipour et al 2013*). However, another study found similar efficacy between the 2 agents at days 15 and 29 after treatment (*Chouela et al 1999*). Results from another study found that after a single application, permethrin was associated with a higher cure rate compared to ivermectin (*Usha et al 2000*).
- A Cochrane review evaluated 15 studies comparing topical permethrin, topical ivermectin, and oral ivermectin for scabies (*Rosumeck et al 2018*). The meta-analysis found no clear differences in rate of complete clearance of scabies between products, with the exception of the rate of complete clearance after 1 week when comparing topical permethrin to oral ivermectin (relative risk 0.65, 95% confidence interval [CI] 0.54 to 0.78). However, at weeks 2 and 4, there was no difference in the rate of complete clearance for that comparison. Rates of adverse events were similar between all evaluated therapies.
- A meta-analysis evaluated 52 studies comparing treatments for scabies to each other or placebo. These treatments included sulfur, benzyl benzoate, lindane, malathion, crotamiton, permethrin, oral or topical ivermectin, synergized pyrethrins, or herbal treatments. The primary outcome was either clinical or microscopic cure. Secondary outcomes included persistent itching and adverse events. Results of the direct meta-analysis demonstrated permethrin to be significantly better at achieving cure than oral ivermectin, lindane and crotamiton at 1 to 2 weeks and 3 to 6 weeks. Oral ivermectin demonstrated better cure rates than lindane. For persistent itching, oral ivermectin was significantly better than benzyl benzoate and lindane; permethrin was significantly better than lindane. No significant differences between treatments were observed in adverse events. According to the network meta-analysis, the highest probability of cure at 3 to 6 weeks was associated with permethrin + oral ivermectin followed by permethrin alone and topical ivermectin. Topical ivermectin followed by permethrin were the highest ranked to reduce persistent itching. The agents with the lowest probability for adverse events were synthetic pyrethrins, malathion, and oral ivermectin. Sulfur ranked highest in the probability for adverse events followed by permethrin + oral ivermectin (*Thadanipon 2019*).

Lice

- Benzyl alcohol has been evaluated in 2 multicenter, randomized, double-blind, vehicle-controlled studies in patients (6 months of age and older) with an active head lice infestation (N = 628). In both studies, 2 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 I was 71.4% in favor of benzyl alcohol (95% CI, 61.8 to 85.7%) and 48.8% (95% CI, 31.1 to 62%) in study II, 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 I and II, respectively; p < 0.001 for both) (*Meinking et al 2010*).
- Permethrin has demonstrated a higher rate of treatment success compared to Lindane in the treatment of lice following a single application (*Brandenburg et al 1986, Bowerman et al 1987, Kalter et al 1987, Taplin et al 1986a*). Compared to the combination of pyrethrins and piperonyl butoxide, permethrin has been shown to be significantly more efficacious (*Carson et al 1988, DiNapoli et al 1988*). Carson et al reported a cure rate of 96.3% for permethrin and a cure rate of 45.2% for the combination of pyrethrins and piperonyl butoxide at 7 days following treatment (p < 0.005) (*Carson et al 1988*). In multiple studies, malathion has been reported to be pediculicidal and ovicidal or had higher rates of cure when compared to permethrin (*Meinking et al 2004, Meinking et al 2007, Roberts et al 2000*).
- Two identical, vehicle-controlled studies demonstrating the safety and efficacy of ivermectin lotion in the treatment of head lice were completed in 781 patients (6 months of age and older) with head lice. The 2 studies showed that a higher percentage of patients treated with ivermectin lotion, without nit combing, were treatment responders (free of live lice at day 2 and through day 8 to the final evaluation at day 15) following a single application compared to vehicle application (combined study results for day 2: 94.9 vs 31.3%, respectively; day 8: 85.2 vs 20.8%, respectively; day 15: 73.8 vs 17.6%, respectively; p < 0.001 for each comparison). (*Pariser et al 2012*).



• Spinosad has been evaluated in 2 randomized, active-controlled trials of 1038 patients aged 6 months or older 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 1 course of treatment, compared to the majority of permethrin-treated patients who required 2 courses of treatment (p values not reported) (*Stough et al 2009*).

CLINICAL GUIDELINES

Scabies

- Current treatment guidelines from the CDC and the AAP state that permethrin 5% cream is the drug of choice for children 2 months of age and older with scabies. Crotamiton is available as another option for adult patients, but frequent treatment failures have been reported with this agent. Oral ivermectin may be considered for patients who fail treatment or for those who cannot tolerate topical therapies. Lindane is not recommended due to the risk of neurotoxicity, and the lotion formulation that was FDA-approved for scabies has been discontinued (*AAP Red Book 2018, CDC 2018, Clinical Pharmacology 2019, Gunning et al 2012, Strong et al 2010, WHO 2019*).
- Crusted scabies should be treated using oral ivermectin in combination with a topical agent (CDC 2018).
- Household members and sexual contacts of the affected individual should be treated even if they do not have any signs of an infestation, as it can take 2 to 5 weeks for symptoms to develop. To prevent re-infestation, all patients should be treated at the same time (*CDC 2018*).
- All clothing, bedding, and towels require decontamination by laundering in hot water and drying in a hot dryer, drycleaning, or sealing in a plastic bag for 72 hours. The use of a fumigant or insecticide spray is not recommended (*CDC* 2018).

Lice

- The CDC and the AAP recommend permethrin 1% as first-line antiparasitic therapy for the treatment of lice. For the treatment of head lice, therapy should be initiated with permethrin 1% or pyrethrins when there is no known resistance. Malathion (in patients 6 years of age or older) and benzyl alcohol (in patients 6 months of age and older) may be used when resistance to permethrin or pyrethrins is documented or when treatment with these products fails despite their correct use. Per the AAP, spinosad and ivermectin might prove helpful in difficult cases, but the cost of these preparations should be taken into account by the prescriber. Lindane is no longer recommended by the AAP for use in treatment of head lice (AAP Red Book 2018, CDC 2015[a], CDC 2015[b], CDC 2016, Devore et al 2015, Downs et al 1999, Gunning et al 2012).
- All clothing, bedding, and towels should be laundered in hot water and dried in a hot dryer to avoid another infestation. Items that cannot be washed can be placed in a hot dryer for 20 to 30 minutes, dry-cleaned, or sealed in a plastic bag for 2 weeks; combs and brushes should be soaked in hot water (at least 130 degrees Fahrenheit) for 5 to 10 minutes. The use of fumigants is not recommended (*CDC 2015/a]*, *CDC 2015/b]*, *CDC 2016*).
- Non-pharmacological tactics should be used to treat body lice, such as laundering clothing and bedding in hot water as well as regular bathing. If the prescriber determines that pharmacological treatment is necessary, the choice of pediculicide should follow the same guidelines as used for head lice (*CDC 2015[a], Gunning et al 2012*).
- The CDC recommends permethrin 1% or the combination of piperonyl butoxide and pyrethrins as equivalent therapies for pubic lice (*CDC 2015[b]*).

SAFETY SUMMARY

- Lindane carries a boxed warning for therapy placement, neurologic toxicity, contraindications, and proper use.
 Lindane should only be used in patients who cannot tolerate or have failed first-line treatment with safer medications.
 - Neurologic toxicity has been reported with Lindane use, including seizures and deaths; use with caution in infants, children, the elderly, individuals with other skin conditions, and individuals who weigh less than 110 pounds (50 kg).
 - Lindane is contraindicated in premature infants and individuals with known uncontrolled seizure disorders.
 - Patients should be instructed on the proper use of Lindane including amount to apply, how long to leave on, and avoiding retreatment.
- Lindane is contraindicated in patients with crusted (Norwegian) scabies and other skin conditions such as atopic dermatitis or psoriasis that may increase systemic absorption of the drug.

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- Malathion lotion is contraindicated in neonates and infants because their scalps are more permeable and may have increased absorption of malathion. Malathion lotion is flammable; patients should be instructed to allow hair to dry naturally after application and avoid use of any electric heat source.
- All topical scabicide and pediculicide products are contraindicated in patients with a sensitivity or allergy to any active or inactive ingredient in the product.
- For the class, adverse events are mostly dermatological in nature.
- Lindane should be used with caution with any drug that is known to lower the seizure threshold. Drug interactions for the remaining products in this class are minimal due to the topical application.
- Products have not been evaluated in the elderly; caution should be exercised when used in this population.

Drug	Pregnancy	Nursing Mothers	Pediatrics
Eurax (crotamiton)	Category C*	Lactation information is not available from the manufacturer so it is unknown whether excreted in breast milk; use with caution.	Safety and effectiveness in pediatric patients have not been established.
Lindane (gamma- hexachlorocyclohexane)	Category C*	Enters breast milk; use is contraindicated. Discard milk for at least 24 hours after application.	Avoid use in infants and young children due to a higher incidence of adverse reactions and risk of toxicity in this age group.
Natroba (spinosad)	Category B*	Spinosad is not present in breast milk. However, Natroba also contains benzyl alcohol which may be systemically absorbed through the skin. Use only if benefits outweigh the risks and discard breast milk for at least 8 hours after use.	Should not be used in children younger than 6 months old due to risk of benzyl alcohol toxicity.
Ovide (malathion)	Category B*	Unknown whether excreted in breast milk; use with caution.	Should not be used in children younger than 6 years old.
Permethrin	Category B*	Unknown whether excreted in breast milk; due to tumorigenic potential in animal studies, consider discontinuing nursing temporarily or withholding the drug while nursing	Should not be used in children younger than 2 months old.
Piperonyl butoxide and pyrethrins	Category C*	Unknown whether excreted in breast milk; use with caution.	Should not be used in children younger than 2 years old.
Sklice (ivermectin)	Unclassified [†] : No studies evaluating use in pregnant women. Observational studies have not revealed adverse effects; but these studies cannot definitively rule out any drug-associated risk.	Following oral administration, it is excreted in human milk in low amounts; this has not been evaluated following topical administration.	Should not be used in children younger than 6 months old.

Table 3. Specific Populations

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Drug	Pregnancy	Nursing Mothers	Pediatrics
Ulesfia (benzyl alcohol)	Category B*	Unknown whether excreted in breast milk, but benzyl alcohol may be absorbed through the skin; use with caution.	Should not be used in children younger than 6 months old.

*Pregnancy Category B = No evidence of risk in humans, but there remains a remote possibility. Animal reproduction studies have failed to demonstrate a risk to the fetus, and there are no adequate and well-controlled studies in pregnant women. Pregnancy Category C = Risk cannot be ruled out. Animal reproduction studies have shown an adverse effect on the fetus and there are no adequate and well-controlled studies in but potential benefits may warrant use of the drug in pregnant women despite potential risks.

†In accordance with the FDA's Pregnancy and Lactation Labeling Rule (PLLR), this product is not currently assigned a Pregnancy Category. Consult product prescribing information for details.

DOSING AND ADMINISTRATION

Table 4. Dosing and Administration

Drug	Available Formulations	Route	Usual Recommended Frequency	Comments
Eurax (crotamiton)	Cream (Eurax), lotion (Eurax)	Topical	Apply thoroughly from chin to toes, including skin folds and under fingernails; a second application is recommended 24 hours later. A cleansing bath should be taken 48 hours after the last application.	
Lindane (gamma- hexachlorocyclohexane)	Shampoo	Topical	Apply to dry hair and leave in place for 4 minutes. Then add a small amount of water until a good lather forms and immediately rinse. Retreatment is not recommended.	
Natroba (spinosad)	Suspension	Topical	Apply to dry scalp and hair; wash off after 10 minutes. A second treatment may be applied after 7 days if live lice are still seen.	
Ovide (malathion)	Lotion	Topical	Apply to dry hair. Leave on 8 to 12 hours then shampoo and rinse. May repeat with a second application after 7 to 9 days if lice are still present.	Product is flammable; avoid smoking, open flame, and hair dryers. Allow hair to dry naturally and uncovered.
Permethrin	Cream, crème rinse, lotion	Topical	Scabies: Apply cream from head to soles of feet. Wash off after 8 to 14 hours. Application may be repeated after 14 days if live mites are still present. Lice: Apply crème rinse/lotion on the scalp and damp hair. Leave on for 10 minutes then rinse with water. May repeat after 7 days if live lice are still present.	The 5% cream formulation is approved for scabies and is available by prescription only; the 1% crème rinse and lotion are approved for head lice and are available OTC.



Drug	Available Formulations	Route	Usual Recommended Frequency	Comments
Piperonyl butoxide and pyrethrins	Shampoo, crème rinse	Topical	Apply to hair and scalp. Leave on for no more than 10 minutes then rinse. Treatment should be repeated after 7 to 10 days on dry hair.	
Sklice (ivermectin)	Lotion	Topical	Apply to dry hair and scalp. Leave on for 10 minutes then rinse with water. Wait 24 hours before using shampoo. For single use only; do not re-treat.	
Ulesfia (benzyl alcohol)	Lotion	Topical	Apply to dry hair and scalp. Leave on for 10 minutes then rinse. Repeat treatment after 7 days.	

See the current prescribing information for full details

CONCLUSION

- There are a number of effective topical scabicide and pediculicide agents available including Eurax (crotamiton), Lindane (gamma-hexachlorocyclohexane), Ovide (malathion), Natroba (spinosad), permethrin (Elimite 5%, NIX 1%), piperonyl butoxide with pyrethrins (RID), Sklice (ivermectin) and Ulesfia (benzyl alcohol). Permethrin is recommended as first-line therapy for treatment of scabies and lice, despite increasing resistance in the United States (*Downs et al 1999, CDC 2016, Devore et al 2015*).
- 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. Ivermectin and spinosad are 2 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 (*Villegas et al 2012*). Ivermectin has been approved for one-time use. Permethrin 1% and the combination of pyrethrins and piperonyl butoxide are available OTC (*CDC 2016*). Lindane, a well-known older agent, is reserved as second-line therapy and carries a boxed warning describing risk of neurotoxicity associated with its use. Other available agents offer alternative options should resistance occur, or if a patient experiences treatment failure with a first-line product (*CDC 2016*, *Devore et al 2015*).
- Limited direct comparisons have been completed with agents in this class. Permethrin has demonstrated a higher rate of treatment success compared to Lindane in the treatment of lice following a single application (*Brandenburg et al 1986, Bowerman et al 1987, Taplin et al 1986a*). 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 (*Carson et al 1988, DiNapoli et al 1988*). Numerous studies have demonstrated a significantly lower cure rate after 4 weeks with Lindane compared to oral ivermectin (*Goldust et al 2013, Madan et al 2001, Mohebbipour et al 2013*); however, one study found no difference at days 15 and 29 following treatments (*Chouela et al 1999*). In multiple studies, malathion has been reported to be pediculicidal and ovicidal when compared to permethrin (*Meinking et al 2004, Roberts et al 2000*).
- The newer agents, which include benzyl alcohol, ivermectin, and spinosad, have shown cure rates (lice-free at day 14 or 15) of 75 to 76%, 71 to 76% and 84.6 to 86.7%, respectively, although there is limited published literature confirming these results.
- 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 Eurax. A meta-analysis demonstrated permethrin to be significantly better at achieving cure than oral ivermectin, lindane and crotamiton at 1 to 2 weeks and 3 to 6 weeks (*Thadanipon 2019*). Current clinical guidelines recommend permethrin 5% as the drug of choice for the treatment of scabies. Lindane is not recommended due to its toxicity, and the lotion formulation that was approved for scabies has been discontinued; the

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shampoo formulation is only approved for lice and should be reserved for patients who have exhausted medication options that pose less risk. For crusted scabies, oral ivermectin should be co-administered with a topical agent.

- Overall, topical pediculicides are effective in eradicating head lice, but generally do not have any effect on ova (nits). The guidelines from CDC and AAP recommend permethrin 1% or the combination of pyrethrins and piperonyl butoxide for head lice when resistance is not suspected (AAP Red Book 2018, CDC 2016, Devore et al 2015). Retreatment of head lice usually is recommended because most approved pediculicides are not completely ovicidal. Spinosad and malathion are the only ovicidal medications for the treatment of head lice, but the need for re-treatment has been reported (CDC 2016). Lindane is no longer recommended by the AAP for the treatment of head lice (Devore et al 2015).
- Body lice can be managed with nonpharmacological tactics such as laundering clothes and bedding in hot water and regular bathing. Should pharmacological treatment be necessary, the choice of pediculicide should follow the same guidelines as used for head lice (*CDC 2015[a], Gunning et al 2012*).
- The CDC recommends permethrin or the combination of piperonyl butoxide and pyrethrins as equivalent therapies for pediculosis pubis (CDC 2015[b]).

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