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Indiana Medicaid Therapeutics Committee **Therapeutic Class Review Summary**

Therapeutic Class:

Topical Antiparasitics

Overview:

The topical antiparasitics are used to treat infestations of head lice and scabies. Head lice infestations are the most common parasitic disease in the developed world. Infections mostly affect school-age children and the incidence of head lice is increasing due to resistance to over-the-counter products. Scabies, often found in nursing facilities and prisons, is an infestation of the skin where the scabies mite burrows into the upper skin layer where it lives and lays eggs. Symptoms include itching and a pimple-like skin rash. The scabies mite is spread by direct, prolonged, skin-to-skin contact.

The topical antiparasitic agents offer varying mechanisms of action against *Sarcoptes scabiei* (scabies) and *Pediculus humanus* (lice). While the exact mechanism of action of crotamiton is not known, we do know that malathion acts by inhibiting cholinesterase, while permethrin and pyrethrins act to disrupt the sodium channel current of the parasites' nerve cell membrane, resulting in paralysis.

The first topical antiparasitic agent available was lindane (1951). Now a second-line agent, and banned from use in some states, lindane has succumbed to safer and more efficacious treatments. With its black box warning regarding neurotoxicity issued in March 2003, use is limited today. The other agents reviewed offer efficacious treatment for scabies and/or head lice. Clinical evidence supports use of permethrin cream over crotamiton and lindane in the treatment of scabies, and use of malathion lotion over lindane and permethrin for head lice infestations. A review of literature comparing permethrin efficacy in the 80's to that in studies from the late 90's indicates growing resistance to this treatment option.

Benzyl alcohol lotion (Ulefsia™) is the first occlusive-based therapy approved for head lice and can be used in children as young as 6 months of age. Benzyl alcohol is not ovicidal; it works by suffocation of the lice, therefore resistance should not occur, and neurotoxicity is not a concern. However, two treatments are required since benzyl alcohol kills lice only and not the nits. This product may be an appropriate option for head lice resistant to permethrin, or where use of a pediculocide is a concern, especially in young children.

Efficacy and safety with the topical antiparasitic agents is directly related to patient adherence with label instructions. Depending on the product, the application times differ and other important instructions may apply. For example, malathion lotion is flammable so patients cannot use electrical hair dryers or smoke during the application. Adverse

events more commonly occur from misuse of the topical agents than when instructions are strictly followed. The agents are well-tolerated, with most common adverse events being skin irritation type reactions. Finally, all products are available with generic formulations, except Eurax® and Ulefsia™. Additionally, Nix® 1% cream rinse (permethrin) is available over-the-counter, along with the topical pyrethrin products.

GENERIC NAME	TRADE NAME	MANUFACTURER	GENERIC
Benzyl alcohol	Ulefsia™	Sciele Pharma	N
Crotamiton	Eurax®	Bristol-Myers Squibb Pharmaceuticals	N
Lindane	Lindane	Morton Grove Pharmaceuticals, others	Y
Malathion	Ovide®	Taro Pharms, Synerx Pharma	Y
Permethrin	Elimite®, NIX®, Acticin®, A-200®	Mylan, Allergan, Clay Park, Hogil, others	Y
Pyrethrins / Piperonyl Butoxide	RID®, A-200®	Hogil Pharmaceutical Corporation, Rugby, Bayer, others	Y

Summary:

The topical antiparasitics are effective for the treatment of scabies (*Sarcoptes scabiei*) and lice (*Pediculus humanus*), including head, body, and crab lice. While some of the reviewed agents have indications for both infections, crotamiton is only indicated for scabies, benzyl alcohol and malathion for head lice, and the pyrethrin agents for head, body, and crab lice. Several of these anti-infectives have been available for many years (E.g. lindane, permethrin, pyrethroids) and as a result, their efficacy has fallen due to resistance. In fact, the available malathion product (Ovide) was re-introduced to the market for this reason. Lindane, the eldest of all of the reviewed agents, should be restricted only to those who have failed first-line treatment with safer alternatives. Additionally, some states have banned lindane due to safety concerns.

Clinical data suggest topical permethrin is most efficacious for the treatment of scabies (compared with lindane or crotamiton), it is available generically, can be used in children as young as 2 months of age and is a pregnancy category B (compared with a C for crotamiton and lindane). One application of permethrin cream is typically curative, whereas a second application of crotamiton is advised 24 hours after the first application. More recent clinical data for the treatment of head lice indicates growing resistance with permethrins and subsequent efficacy with malathion. Data even suggest efficacy of malathion when applied for less than the recommended 8-12 hour timeframe. However,



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patients must be careful with application of malathion lotion because it is flammable. Benzyl alcohol lotion is the first occlusive-based therapy approved for head lice and can be used in children as young as 6 months of age. Benzyl alcohol is not ovicidal therefore resistance and neurotoxicity are not a concern. However, two treatments are required since benzyl alcohol kills lice only and not the nits. This product may be an appropriate option for head lice resistant to permethrin, or where use of a pediculocide is a concern, especially in young children.

In general, the topical antiparasitic agents are well-tolerated when applied according to product label recommendations. The most common adverse events reported are related to skin exacerbations of pruritus, itching, tingling, rash, and irritation. The criteria for selection of an agent for the preferred drug list should include consideration of indications, safety, efficacy, and cost.