Pityriasis Versicolor
A Systematic Review of Interventions
Stephanie W. Hu, MD; Michael Bigby, MD

Objective To determine the efficacy of topical or systemic agents in the treatment and prevention of pityriasis versicolor.

Design Systematic review and meta-analysis.

Data Sources The Cochrane Skin Group Specialized Register (to June 2008), Cochrane Central Register of Controlled Trials, MEDLINE (1950 to June 2008), EMBASE (1974 to June 2008), LILACS (to March 2009), the gray literature, and sources for registered trials to November 2008. Reference lists of all retrieved trials and review articles were checked for additional trials.

Study Selection Controlled trials that examined therapies used in children or adults with a clinical or microscopic diagnosis of pityriasis versicolor.

Data Extraction The primary outcome measure included a negative result from mycological evaluation of participants with direct microscopy using potassium hydroxide smear. The secondary outcome measures were findings from Wood's light examination and a negative clinical evaluation result, with disappearance of visual signs (except pigmentary defects) and symptoms.

Data Synthesis Results of treatment and prevention of pityriasis versicolor infection in 8327 participants in 93 controlled trials were examined. Overall, trials investigating the efficacy of therapeutic and prophylactic treatments for pityriasis versicolor are poorly reported and may be of low quality. Most trials did not adequately report the methods of randomization, concealment of allocation, and blinding, and many did not use intention-to-treat analysis. Most topical treatments used to treat pityriasis versicolor are effective compared with placebo, with numbers needed to treat of 1 to 3. Data suggest that longer durations of treatment and higher concentrations of active agents produce greater cure rates.

Conclusions Most topical and systemic treatments used for pityriasis versicolor are effective compared with placebo. Randomized controlled clinical trials are needed to establish relative efficacy of topical and systemic agents used for treatment and prevention of pityriasis versicolor.

COMMENT
A number of options are currently available for the treatment of pityriasis versicolor, and both topical and oral medications have been shown to be effective. Most topical treatments are effective compared with placebo, but the data are less conclusive for topical treatments compared with one another and with differing dosages and durations. Overall, longer durations of treatment and higher concentrations of active agents appear to produce greater cure rates (eTable 1 and Figures 1-5).

Although optimal regimens have not been established, the data suggest that 1 to 4 weeks of treatment can be recommended. Ketoconazole shampoo is applied to affected areas, left on for 5 to 10 minutes, and then washed off. Treatment is repeated daily for 1 to 4 weeks. The imidazole creams are applied once or twice daily for 1 to 4 weeks. Selenium sulfide or zinc pyrithione shampoo is applied to affected areas for 5 to 10 minutes and then showered off, and treatment is repeated daily for 1 to 4 weeks (eTable 1).

Data suggest that extensive pityriasis versicolor can be successfully and safely treated with the oral imidazole antifungal agents, including ketoconazole, 200 mg/d for 10 days, itraconazole, 200 mg/d for 7 days or 100 mg/d for 2 weeks, or fluconazole, 300 mg/wk for 2 to 4 weeks.

Given their ability to inhibit the cytochrome P-450 system, all of the systemically absorbed imidazole antifungal agents have the potential to induce drug-drug interactions. Itraconazole in particular appeared to cause gastrointestinal symptoms across multiple trials, including nausea, vomiting, abdominal pain, flatulence, and elevated alanine aminotransferase and aspartate aminotransferase levels. Concomitant administration with cisapride, pimozide, quinidine, dofetilide, or levomethadyl is contraindicated because of rare cases of serious cardiovascular adverse events (including death,
ventricular tachycardia, and torsades de pointes) occurring from increased levels of these drugs induced by itraconazole. Itraconazole also carries a black box warning from the US Food and Drug Administration (FDA) for association with development of congestive heart failure (CHF), particularly in patients with a history of CHF. In addition, itraconazole has been associated with rare cases of serious hepatotoxicity (including fatal cases within the first week of treatment). It is, therefore, not recommended to use itraconazole in patients with active liver disease, elevated liver enzyme level, or prior hepatotoxic reactions to other drugs. In clinical trials, its use has been associated with, in decreasing frequency, nausea, cutaneous eruption, vomiting, pruritus, headache, edema, hypertension, diarrhea, abnormal liver function test results, hypokalemia, fever, dizziness, abdominal pain, anorexia, fatigue, malaise, decreased libido, hypertriglyceridemia, and albuminuria. Ketoconazole carries a black box warning issued by the FDA because it has been associated with fatal hepatotoxicity. The frequency is low (134 cases per 100,000 person-months [95% CI, 37-488] in one study), but it is the highest among the oral imidazole antifungal agents. Liver function test results should be monitored if the duration of treatment exceeds 1 week. Like itraconazole, ketoconazole also carries a black box warning that precludes concomitant use with cisapride. In addition, high doses of ketoconazole may suppress adrenocortical function. In clinical trials, nausea and/or vomiting, pruritus, and abdominal pain were reported. Diarrhea, dizziness, fever, gynecomastia, and headache occur less frequently. Ketoconazole significantly inhibits the cytochrome P-450 system and plays a major role in many drug interactions. Fluconazole has been associated with headache, nausea, abdominal pain, diarrhea, cutaneous eruption, and vomiting in clinical trials. Hepatitis and elevated liver function test results are rare and less common than with other imidazoles. Serious adverse reactions are rare. Data for prevention of recurrences are sparse. One randomized clinical trial of 50 participants suggests that itraconazole, 200 mg twice daily once per month for 6 months, is effective in preventing recurrences. Optimal regimens for ketoconazole and fluconazole, as well as for topical agents, have not been established. Although many topical and systemic therapies may in fact be effective, it can be difficult to compare the results of the studies owing to significant heterogeneity in study design and agents examined. It is thus important for future studies to be conducted and written in a manner that facilitates an easier comparison between studies. For the studies we have included on the treatment of pityriasis versicolor, we have performed critical evaluations of their quality and design to assess the degree of validity, reliability, and generalizability of the results. The main quality criteria assessed included adequate methods of randomization, concealment of allocation, blinding, and ITT analysis of the data. Randomization and concealment of allocation minimize bias in patient selection and allocation. Blinding and ITT analysis minimize bias in the assessment of patients and evaluation of the data, respectively. The lack of reporting of methods made the determination of study quality difficult. The only information provided in most trials we evaluated was that "randomized controlled clinical trial," "blind," or "double blind" appeared in the title, abstract, or methods sections. Despite the claim of randomization and blindness in many studies, adequate methods of randomization and blinding may not be used. We therefore considered a study to be randomized, concealed, and blinded if adequate methods were described. We gave credit for ITT analysis if ITT was performed or enough primary data were provided for us to perform ITT analysis. The adequacy of randomization was the greatest source of disagreement between us in judging the quality of trials. Ultimately, owing to the poor reporting of methodology, the overall quality of the trials may have been better than that which we reported. Current data provide strong evidence on the efficacy of topical and systemic agents in the treatment of pityriasis