Economic Analysis of Oral and Topical Therapies For Onychomycosis of the Toenails and Fingernails

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ABSTRACT

Objective: Several antifungal agents are indicated for onychomycosis, a fungal infection of the toenails and fingernails. These agents differ in their dosing regimen, efficacy, adverse events profile, potential for drug interaction, and cost. We conducted a pharmacoeconomic analysis of oral and topical therapies for onychomycosis from the perspective of a hypothetical managed care payer to determine the most cost-effective agent.

Design: A decision analytic model was developed to evaluate the pharmacoeconomic profiles of itraconazole–continuous (Sporanox, Janssen Pharmaceutica), itraconazole–pulse (Sporanox, Janssen Pharmaceutica), terbinafine (Lamisil, Novartis Pharmaceuticals), and ciclopirox (Penlac, Dermik Laboratories) in the treatment of fingernail and toenail onychomycosis.

Methodology: We conducted a meta-analysis of the available literature to populate the decision analytic model with clinical point estimates for success, failure, and relapse. A panel of expert dermatologists defined resources consumed during the onychomycosis treatment process. These resources were then assigned values, using publicly available data sources, to reflect the U.S. managed care perspective. These clinical and economic data elements were integrated in the decision analytic model to arrive at the expected cost of treatment for each drug. Additionally, incremental cost-effectiveness was calculated for treatment success and disease-free days achieved by each therapy. Finally, a policy-level analysis of the budgetary impact of using the therapies for onychomycosis in a managed care setting was conducted.

Results: The meta-analysis demonstrated terbinafine to be the therapeutic alternative with the highest success rate for both fingernails (96.55 percent) and toenails (81.15 percent). Terbinafine also had the lowest relapse rate (6.42 percent) and the highest number of disease-free days for both fingernails and toenails. Subsequently, in terms of cost-effectiveness, terbinafine dominated all other comparators for fingernails and toenails.

Conclusions: Based on the patient-level analysis, we concluded that terbinafine is the most cost-effective therapy in the treatment of onychomycosis from a managed care perspective. Furthermore, at the policy level, increased utilization of terbinafine among onychomycosis patients is likely to reduce the managed care organizations’ per member per month cost.

Key words: onychomycosis, itraconazole, Sporanox, terbinafine, Lamisil, ciclopirox, Penlac, pharmacoeconomics, meta-analysis

INTRODUCTION

Onychomycosis is a fungal infection of the toenails and fingernails, with the former more commonly affected. Dermatophytes, such as those of the genera Epidermophyton, Microsporum, and Trichophyton, are estimated to be involved in up to 95 percent of onychomycosis infections (Summerbell 1989). Nondermatophyte origins are less common and include molds and yeasts, such as Candida albicans.

Onychomycosis generally affects men and women in equal proportions, with estimates of overall prevalence reported in the literature varying widely, from 2.6 percent (Sais 1995) to 13.4 percent (Elewski 1997a). The prevalence is much higher in certain populations, such as the elderly and those with immunosuppressive conditions (Levy 1997). This disease can result in permanent nail deformity and can be a source of embarrassment and reduced self-esteem for the infected patient (Drake 1995, Lubeck 1993, Schein 1997).

The rationale for treating onychomycosis goes far beyond patients’ cosmetic complaints, however. Toe-nail onychomycosis takes many months to control and, during this time, causes pain and can make walking difficult. Therefore, onychomycosis treatment is necessary to overcome physical limitations, reduce the spread of infections, and reduce pain.

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Some populations are at higher risk for developing more serious complications due to the disease. For example, diabetes patients are at a threefold higher risk of secondary infection, gangrene, and foot ulcers, compared with diabetes patients without onychomycosis (Boyko 1999). Immunocompromised patients can develop widespread cutaneous infections that are resistant to topical therapy (Radentz 1989). Clinical success also is affected by the location of the infection, in that fingernail infections are usually cured more easily and quickly than toenail infections (Goldfarb 1960).

Newer agents like ciclopirox (Penlac) have been added as therapeutic choices for onychomycosis. Although onychomycosis treatment with oral antifungal agents is associated with elevated drug costs, oral treatment stands above other alternatives on the basis of its higher mycological and clinical cure rates (Brautigam 1996, Tom 1999, Gupta 1998, Evans 1999).

In a study comparing oral and topical therapies through 9-months of clinical care, toenail treatment using oral agents generated higher costs when compared with treatment using topical agents (Stier 2001). Nevertheless, the cost of oral antifungal treatment is outweighed by its increased clinical effectiveness, lower toxicity, and reduced treatment time (Ling 1998, Scher 1998).

Several economic analyses have been published examining oral and topical antifungal agents in the treatment of onychomycosis (Marchetti 1996, Arkian 1994, Einarson 1994, Einarson 1995b, Davis 1995, Gupta 2000a, Joish 2001). These studies relied on similar model structures and data from clinical trials. Recently, more information has been published on the efficacy of these drugs and newer drugs that have become available in the treatment of onychomycosis; these efficacy data have been included in the present analysis.

To assess the cost-effectiveness of these agents, we conducted a comprehensive pharmacoeconomic and policy analysis of oral and topical therapies for onychomycosis from a managed care perspective in the United States.

**METHODS**

A decision analytic model was developed to assess various treatment modalities for onychomycosis. This model structure was developed utilizing available clinical data with the guidance of a panel of practicing dermatologists and onychomycosis experts. The decision analytic model was populated using clinical data derived through a meta-analysis, resource utilization data determined by the expert panel, and resource value data provided by public data sources (see original models in Marchetti 1996). Meta-analysis was then performed on data from 3,248 patients.

**TABLE 1 Criteria for efficacy study identification**

<table>
<thead>
<tr>
<th>Inclusion criteria</th>
<th>Exclusion criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult patients</td>
<td>Onychomycosis caused by yeast or mold*</td>
</tr>
<tr>
<td>Onychomycosis or tinea unguium caused by dermatophytes</td>
<td>Immunocompromised patients</td>
</tr>
<tr>
<td>Success defined as mycological cure only</td>
<td>Patients with concurrent psoriasis of the nails</td>
</tr>
<tr>
<td>Dosage and treatment lengths within currently suggested ranges</td>
<td></td>
</tr>
<tr>
<td>Success recorded as per protocol</td>
<td></td>
</tr>
</tbody>
</table>

*Three studies that reported less than 3 percent of the total study population with yeast were included.

A comprehensive literature search in both MEDLINE and EMBASE was undertaken to identify all papers published from 1985 through 2001 on the treatment of onychomycosis with itraconazole–pulse, itraconazole–continuous, terbinafine, and ciclopirox. Abstract retrieval was restricted to studies reported in English (or with an English abstract).

Inclusion and exclusion criteria are reported in Table 1. Of all the studies identified in the search, 44 were excluded for various reasons (Table 2). As a result, 40 clinical trials were used in the analysis. Those trials reported data from 3,248 patients.

An attempt was made to use only randomized, double-blind, comparative trials in an effort to minimize bias. Because many of the trials were open-label, however, a limited number of such trials were assessed and subsequently included in the analysis for terbinafine and itraconazole for fingernail and relapse data. Heterogeneity tests were conducted to minimize bias in the results. Two separate investigators carried out data extraction independently, and consensus was reached through discussion.

Meta-analysis was then performed on extracted data to summarize rates across all available literature. Relevant clinical outcomes included success, failure, or relapse. Success was defined as mycological cure, defined as a negative microscopy examination in potassium...
Cost-of-regimen analysis

Cost of regimen is a calculation of all direct medical costs for each treatment regimen, including DAC. Direct costs represent the amount expended on medical services. In this analysis, direct costs were segmented into the following categories: drug, routine medical care (including laboratory testing), and adverse events management. Drug cost consisted of the DAC (described above), while routine medical care costs consisted of all the visits, procedures, and tests necessary for treatment and monitoring. Adverse events management costs were calculated as a function of resources consumed in treating the event and the incidence of the event. Clinical parameters and indirect costs were not included in this calculation. Financial data included public and proprietary sources (i.e., HCFA, NCHS, and UCR fee schedules) (PMIC 1997).

Expected-cost analysis

The cost-of-regimen analysis described above is a necessary step in economic modeling, but it is somewhat misleading because it does not account for clinical outcomes. Expected-cost analysis addresses this issue by incorporating outcomes into the calculations. In this analysis, the total net cost of each treatment is adjusted to account for the cost of additional therapy when treatment fails or relapse occurs, as determined in the intent-to-treat model. Expected cost represents the product of the probabilities of each outcome and the cost per patient treated.

Disease-free days

Due to the lack of prospectively determined quality-of-life (QoL), data for onychomycosis, disease-free days (DFDs) were used as a proxy for QoL. DFDs constitute the timeframe from clinical success to either relapse or arrival at endpoint of the therapeutic time horizon (i.e., 2 years for fingernail or 3 years for toenail) (Arikian 1994). Expected cost per DFD was calculated by dividing total expected cost of each therapy by total number of DFDs for each treatment.
calculated the relative cost-effectiveness ratio for each therapy by comparing each drug’s cost-effectiveness ratio to the most cost-effective drug.

Policy analysis
The perspective of this analysis was that of the U.S. managed care payer. To facilitate policy-level decision making, we conducted a net economic (budget) impact analysis that detailed population (membership) level implications of each treatment selection. A three-step approach was used for this policy-level analysis. First, the expected cost of treatment per onychomycosis patient was calculated; next, the direct cost (to managed care) of onychomycosis treatment was determined using a treated-prevalence approach. Treated prevalence was calculated in the following manner:

1) Determine the number of covered lives in the plan; \( N_L \)

2) Estimate onychomycosis prevalence in the plan based on published epidemiology data; \( P_O \)

3) Determine total patients in the plan that are expected to have onychomycosis at any given time; \( (N_L * P_O) \)

4) Estimate the percent of members with onychomycosis who typically receive treatment paid by the plan; \( P_T \)

5) Determine the total patients treated; \( [(N_L * P_O) * P_T] \)

Finally, the net budget impact of each drug at different utilization rates was evaluated for the managed care payer at the membership level.

Sensitivity analysis
A sensitivity analysis was performed to test assumptions implicit in the model. Rank order stability analysis (ROSA) (Einarson 1995a), a univariate break-even analysis, was conducted for key model variables including success rates, drug prices, medical care cost, and length of treatment. Additionally, efficacy rates were varied randomly within the 95 percent confidence interval (as defined by the meta-analysis) based on a truncated normal distribution. Financial values were varied randomly within +/- 15 percent of the estimated cost based on a uniform distribution.

RESULTS

Meta-analysis
Onychomycosis of the fingernail. In general, clinical success rates were higher for fingernail than for toenail onychomycosis (Table 4). As published data were unavailable for ciclopirox in fingernail treatment, the average improvement observed between toenail and fingernail for the other agents was used to estimate ciclopirox efficacy in fingernail. More specifically, a 34.28 percent improvement rate was applied over the toenail efficacy rate of ciclopirox (32.08 percent), which resulted in a 43.07 percent efficacy rate for ciclopirox in fingernail. The investigators have used the relative efficacy for oral agents as a conservative proxy, given that the only other reasonable assumption would be that the efficacy was the same in fingernails as in toes, and this was deemed to be an unfair assumption for Penlac. Furthermore, this is a conservative assumption, because in all likelihood, a topical treatment applied to the hands is less convenient than the toes.
making treatment of the fingernails more difficult with topical agents (i.e., lower than expected efficacy). This same disadvantage in treating fingernails would not apply to oral agents.

Overall, terbinafine had the highest success rate (96.5 percent) of the four drugs examined for the primary treatment of onychomycosis of the fingernail, followed by itraconazole–continuous (92.6 percent), itraconazole–pulse (79.3 percent), and ciclopirox (43.1 percent).

**Onychomycosis of the toenail.** Terbinafine had the highest success rate (81.1 percent), followed by itraconazole–continuous (64.5 percent), itraconazole–pulse (56.5 percent), and ciclopirox (32.1 percent).

A total of 17 studies presented data from 494 patients for relapse. Terbinafine had the lowest relapse rate (6.42 percent), followed by itraconazole–pulse (17.60 percent), ciclopirox (20.70 percent), and itraconazole–continuous (26.38 percent).

A total of 26 studies presented data from 2,252 patients for adverse drug reactions. As it was deemed more appropriate to use the adverse event rates reported in the package insert

### TABLE 4 Summary of success and relapse rates

<table>
<thead>
<tr>
<th>Drug</th>
<th>Infection site</th>
<th>Patients</th>
<th>Trials</th>
<th>References</th>
<th>Mean (SE)</th>
<th>95% CI limits</th>
</tr>
</thead>
<tbody>
<tr>
<td>Itraconazole–continuous</td>
<td>Fingernail</td>
<td>61</td>
<td>4</td>
<td>Hay 1987, Hay 1988, Walsoe 1990 (2 groups)</td>
<td>0.926 (0.054)</td>
<td>0.82–1</td>
</tr>
<tr>
<td></td>
<td>Toenail</td>
<td>763</td>
<td>13</td>
<td>Arenas 1991, Arenas 1995, Brautigam 1998, De Backer 1996, Degreffer 1999,</td>
<td>0.645 (0.060)</td>
<td>0.52–0.77</td>
</tr>
<tr>
<td></td>
<td>Relapse</td>
<td>175</td>
<td>7</td>
<td>Arenas 1995, Hay 1987, Hay 1988 (2 groups), Jones 1996, Piepponen 1992, Walsoe 1990</td>
<td>0.263 (0.068)</td>
<td>0.13–0.4</td>
</tr>
<tr>
<td>Itraconazole–pulse</td>
<td>Fingernail</td>
<td>84</td>
<td>3</td>
<td>Odom 1997b, Tosti 1996, Wang 1999</td>
<td>0.793 (0.044)</td>
<td>0.71–0.88</td>
</tr>
<tr>
<td></td>
<td>Toenail</td>
<td>692</td>
<td>11</td>
<td>De Doncker 1996 (2 groups), Ginter 1998, Gupta 2000b, Gupta 2001, Hayu 1997,</td>
<td>0.565 (0.044)</td>
<td>0.36–0.77</td>
</tr>
<tr>
<td></td>
<td>Relapse</td>
<td>34</td>
<td>2</td>
<td>De Doncker 1996 (2 groups)</td>
<td>0.176 (0.065)</td>
<td>0.05–0.3</td>
</tr>
<tr>
<td></td>
<td>Relapse</td>
<td>285</td>
<td>8</td>
<td>Arenas 1995, Baudraz-Rosselet 1992 (2 groups), Goodfield 1992 (2 groups), Hofmann 1995, Honeyman 1997, van der Schroeff 1992</td>
<td>0.064 (0.014)</td>
<td>0.04–0.09</td>
</tr>
<tr>
<td>Ciclopirox</td>
<td>Fingernail</td>
<td>NA</td>
<td>NA</td>
<td>Penlac package insert 2001</td>
<td>0.431</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>Toenail</td>
<td>220</td>
<td>2</td>
<td>Penlac package insert 2001</td>
<td>0.321 (0.035)</td>
<td>0.25–0.39</td>
</tr>
<tr>
<td></td>
<td>Relapse*</td>
<td>NA</td>
<td>NA</td>
<td>Penlac package insert 2001</td>
<td>0.207</td>
<td>NA</td>
</tr>
</tbody>
</table>

CI = confidence interval; NA = not available

*Incremental average of all drugs (34.28 percent)
where available, these rates were used for itraconazole–continuous, itraconazole–pulse, and terbinafine (Table 5). No adverse events leading to discontinuation of ciclopirox treatment were reported. As a result, for itraconazole–continuous, the most common reactions were elevated liver enzymes (4.0 percent) and rash (3.0 percent). With terbinafine, the most commonly reported adverse events were rash and visual disturbance (both 0.9 percent).

**Cost-of-drug and cost-of-regimen analyses**

Table 3 illustrates the dosage, cost per unit, overall DAC, and cost of regimen for all comparators. The DAC for terbinafine in toenails and fingernails was $701 and $351, respectively. Itraconazole–continuous was the highest for toenail ($1,307) and fingernail ($654). Terbinafine demonstrated a regimen cost of $1,106 in toenails and $666 in fingernails, while itraconazole–continuous proved the highest in toenail ($1,783) and fingernail ($1,070). A breakdown of the regimen cost indicates that medical care is a significant contributor of cost to the treatment of both toenails and fingernails across comparators.

**Expected-cost analysis**

Terbinafine had the lowest overall expected cost ($755) for fingernail infections, followed by ciclopirox ($854), itraconazole–pulse ($1,136) and itraconazole–continuous ($1,395). Terbinafine also had an overall expected cost of $1,574 for toenail infections, closely following ciclopirox ($1,568), and lower than itraconazole–pulse ($1,796), and itraconazole–continuous ($2,566).

**Disease-free days**

Table 6 summarizes the expected disease-free days (DFDs) for each treatment comparator. In summary, terbinafine treatment yielded the highest number of DFDs (844) for toenail infections followed by itraconazole–continuous (817), itraconazole–pulse (805), and ciclopirox (511). Terbinafine treatment also yielded the highest number of DFDs (622) for fingernail infections, followed by itraconazole–pulse (594), itraconazole–continuous (562), and ciclopirox (452).

**Cost-effectiveness analysis**

Terbinafine was the most cost-effective alternative, as demonstrated by the relative cost-effectiveness analyses (Table 6). That is, terbinafine had the lowest expected cost per patient while providing a superior success rate and more DFDs to toenail and fingernail patients. Subsequently, terbinafine provided the most favorable average cost per disease-free day ratio ($1.86/DFD) for toenail, followed by itraconazole–pulse ($2.23/DFD), ciclopirox ($3.07/DFD), and itraconazole–continuous ($3.14/DFD). Terbinafine also provided the most favorable average cost per disease-free day ratio ($1.21/DFD) for fingernail, followed by ciclopirox ($1.89/DFD), itraconazole–pulse ($1.91/DFD) and itraconazole–continuous ($2.48/DFD).

**Policy analysis**

We utilized data from a hypothetical managed care plan consisting of 1,010,000 covered lives in the budget impact matrix. Of this population, it was estimated that 4 percent (n=40,400) suffer from onychomycosis and are potential candidates for treatment therapy. A conservative assumption of 10 percent of patients receiving therapy was made for the analysis.

According to epidemiologic data, about 80 percent of onychomycosis infections affect the toenails, and 20 percent affect the fingernails. Although patients often present with both toenail and fingernail infection, to be conservative, we have assumed mutual exclusivity. This translates to 3,232 patients being treated for toenail infections and 808 patients treated for fingernail infections in our representative plan membership population. Using these data, we calculated annual cost per patient and total annual budget for onychomycosis (Figure 1). Additionally, increasing utilization of terbinafine from 0 percent to 100 percent for the treated population is expected to yield total annual savings of $535,165. In other words, if the plan utilized terbinafine 0 percent of the time, it would incur a total annual treatment cost of $2,529,849 or $0.21 per member per month (PMPM). Switching entirely to terbinafine (100 percent terbinafine utilization) from all other antifungal utilization would reduce total annual treatment cost to $1,994,684 or $0.16 PMPM (Figure 2). Results of this analysis suggest that

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**TABLE 5** Adverse events leading to temporary or permanent treatment discontinuation

<table>
<thead>
<tr>
<th>Adverse events</th>
<th>Percent reported</th>
</tr>
</thead>
<tbody>
<tr>
<td>Terbinafine</td>
<td></td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>0.4</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>0.6</td>
</tr>
<tr>
<td>Dyspepsia</td>
<td>0.4</td>
</tr>
<tr>
<td>Headache</td>
<td>0.2</td>
</tr>
<tr>
<td>Liver enzyme abnormalities ≥2× upper limit of normal range</td>
<td>0.2</td>
</tr>
<tr>
<td>Nausea</td>
<td>0.2</td>
</tr>
<tr>
<td>Pruritus</td>
<td>0.2</td>
</tr>
<tr>
<td>Rash</td>
<td>0.9</td>
</tr>
<tr>
<td>Taste disturbance</td>
<td>0.2</td>
</tr>
<tr>
<td>Visual disturbance</td>
<td>0.9</td>
</tr>
<tr>
<td>Itraconazole–continuous</td>
<td></td>
</tr>
<tr>
<td>Liver enzyme abnormalities</td>
<td>4.0</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>4.0</td>
</tr>
<tr>
<td>Headache</td>
<td>1.0</td>
</tr>
<tr>
<td>Hypertension</td>
<td>2.0</td>
</tr>
<tr>
<td>Malaise</td>
<td>1.0</td>
</tr>
<tr>
<td>Myalgia</td>
<td>1.0</td>
</tr>
<tr>
<td>Orthostatic hypertension</td>
<td>1.0</td>
</tr>
<tr>
<td>Rash</td>
<td>3.0</td>
</tr>
<tr>
<td>Vasculitis</td>
<td>1.0</td>
</tr>
<tr>
<td>Hypertriglyceridemia</td>
<td>3.0</td>
</tr>
<tr>
<td>Rash/pruritus</td>
<td>3.0</td>
</tr>
</tbody>
</table>
terbinafine is the least costly therapy for onychomycosis from a managed care perspective.

**Sensitivity analysis**

ROSA demonstrated stability across all scenarios. For example, for terbinafine to be displaced as having the lowest expected cost for the treatment of toenail onychomycosis, its total DAC would have to exceed $1,102.70 or be below $686.09. Conversely, the total DAC for itraconazole–continuous would have to decrease from $1,307.04 to $649.06 for the results of this analysis to change. The DAC for itraconazole–pulse would have to decrease from $653.52 to $450.21. Results are more sensitive to the efficacy of terbinafine as compared with the efficacy of the other agents because its reduced cost of failure causes a lower expected cost.

**DISCUSSION**

In treating onychomycosis, this study clearly confirms previous reports that demonstrate terbinafine to be economically superior to the oral and topical therapies evaluated in this analysis. There are studies that highlight the cost-effectiveness of itraconazole vs. “other” therapies. Nevertheless, the investigators know of no publications that claim that itraconazole is more cost-effective than terbinafine. Itraconazole has been shown to be more cost-effective than agents such as griseofulvin and even fluconazole, due to their lower reported cure rates. Yet this is not necessarily the case with terbinafine, mainly because costs are relatively similar while the cure rates associated with terbinafine are reportedly higher (Darkes 2003, Jansen 2001).

The fungicidal property of terbinafine has produced clinical advantages that are reflected in higher success rates and lower relapse rates for both fingernail and toenail infections. Terbinafine is primarily fungicidal in its mode of action, whereas itra-

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**TABLE 6** Calculation of total disease-free days and cost-effectiveness analysis of onychomycosis therapy, expressed as cost per disease-free day

<table>
<thead>
<tr>
<th></th>
<th>Itraconazole–continuous</th>
<th>Itraconazole–pulse</th>
<th>Terbinafine</th>
<th>Ciclopirox</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Toenail</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disease-free days (DFDs)</td>
<td>817</td>
<td>805</td>
<td>844</td>
<td>511</td>
</tr>
<tr>
<td>Cost/DFD</td>
<td>$3.14</td>
<td>$2.23</td>
<td>$1.86</td>
<td>$3.07</td>
</tr>
<tr>
<td>Relative cost-effectiveness compared with terbinafine</td>
<td>1.68</td>
<td>1.20</td>
<td>1.00</td>
<td>1.65</td>
</tr>
<tr>
<td><strong>Fingernail</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DFDs</td>
<td>562</td>
<td>594</td>
<td>622</td>
<td>452</td>
</tr>
<tr>
<td>Cost/DFD</td>
<td>$2.48</td>
<td>$1.91</td>
<td>$1.21</td>
<td>$1.89</td>
</tr>
<tr>
<td>Relative cost-effectiveness compared with terbinafine</td>
<td>2.04</td>
<td>1.58</td>
<td>1.00</td>
<td>1.59</td>
</tr>
</tbody>
</table>

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**FIGURE 1** Budget impact analysis

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ITR-C = itraconazole–continuous, ITR-P = itraconazole–pulse, TER = terbinafine, CIX = ciclopirox
conazole is primarily fungistatic. Terbinafine provides superior long-term mycological and clinical efficacy and lower rates of mycological and clinical relapse compared with intermittent itraconazole (Sigurgeirsson 2002).

Aside from the economic advantage to the payer, there are advantages to the patient. The reduced length of treatment, as compared with newer drugs such as ciclopirox, encourages higher rates of compliance with treatment regimens that yield higher efficacy rates. The fewer relapses associated with terbinafine in comparison with itraconazole—continuous, itraconazole—pulse, and ciclopirox allow the patient more disease-free days, which lead to a presumed improvement in patient quality of life.

The validity of the outcomes of this analysis depends on the quality of the inputs. We used the best available evidence to estimate success rates for these drugs, using randomized controlled trials where available. In all cases, results were verified with an expert panel of practicing dermatologists. The meta-analysis used standard techniques, including use of two independent evaluators and the more conservative random effects model.

Additionally, differences in real-world settings can affect results of the analysis. For example misdiagnosis can result in prescribing for inappropriate patients, as well as underdiagnosis that results in patients not being treated. Though these circumstances can lead to variations in cost results, they have not been considered in this analysis due to lack of data.

Sensitivity analysis indicates that calculations were robust against perturbations in assumptions and estimations regarding model inputs. For all plausible values, terbinafine remained the treatment alternative demonstrating the lowest expected cost for the treatment of onychomycosis. The specifics of other health care settings should be examined, however.

**CONCLUSION**

This study confirms the results of previous pharmacoeconomic analyses of onychomycosis, that terbinafine is the most cost-effective choice for treating onychomycosis. For both fingernail and toenail infections, terbinafine dominated all treatment alternatives evaluated in the decision analytic model. Pharmacoeconomic dominance provides evidence for adopting terbinafine as the drug of choice for the treatment of onychomycosis.

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**DISCLOSURE OF RELATIONSHIPS**

Neil Shear, MD, has been a consultant for Janssen Pharmaceutica and is currently a consultant for Novartis Pharmaceuticals Corp. Kristijan Kahler is an employee of Novartis Pharmaceuticals.

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