Pharmacoeconomic analysis of the new oral antifungal agents used to treat toenail onychomycosis in the USA

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Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
New oral antifungal agents - itraconazole (pulse and continuous), terbinafine, and fluconazole, used to treat toenail onychomycosis in the USA.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
Patients with toenail onychomycosis in the USA.

Setting
Hospital and community. The economic study was set in the USA.

Dates to which data relate
Effectiveness and resource use data were collected from studies published between 1990 and 1999. Cost data were collected from a 1998 source and from discussions with physicians who manage onychomycosis. Prices referred to 1998/1999.

Source of effectiveness data
Effectiveness data were derived from a review of the literature and discussions with physicians who manage onychomycosis.

Modelling
A 3-year decision tree was used to determine the cost-effectiveness of the various oral antifungal drugs.

Outcomes assessed in the review
The review assessed mycologic cure rates, clinical response rates, and relapse rates.

Study designs and other criteria for inclusion in the review
The review included randomised blinded studies and non-randomised studies enrolling more than 50 patients.
Sources searched to identify primary studies
The MEDLINE and EMBASE databases were searched from 1966 to August 1999. Relevant English language articles and information presented at educational meetings were used.

Criteria used to ensure the validity of primary studies
Only those studies that reported efficacy data in immunocompetent individuals with dermatophyte onychomycosis of the toenails were considered. No adjunctive oral antifungal therapy was allowed while the patient was receiving oral antifungal treatment.

Methods used to judge relevance and validity, and for extracting data
Not reported.

Number of primary studies included
At least 39 studies were included in the review.

Methods of combining primary studies
A meta-analysis was used to combine primary studies. Data were combined using the method based on that of DerSimonian and Laird (1986), and modified by Velanovich (1991) for single-group analysis.

Investigation of differences between primary studies
Not stated.

Results of the review
The results of the review were as follows:

The mycologic cure rate was 41.1 (95% CI: 1.2-81.0) with griseofulvin, 65.5 (95% CI: 55.5-75.5) with itraconazole (continuous), 71.1 (95% CI: 61.4-80.9) with itraconazole (pulse), 77.2 (95% CI: 69.3-85.1) with terbinafine, and 65.6 (95% CI: 51.7-79.5) with fluconazole.

The clinical response rate was 33.7 (95% CI: 6.1-61.4) with griseofulvin, 69.0 (95% CI: 59.3-78.6) with itraconazole (continuous), 74.7 (95% CI: 66.9-82.5) with itraconazole (pulse), 75.3 (95% CI: 69.6-81.0) with terbinafine, and 66.5 (95% CI: 43.6-89.5) with fluconazole.

The relapse rate was 40 with griseofulvin, 21 with itraconazole (continuous), 10.4 with itraconazole (pulse), 15 with terbinafine, and 4.8 with fluconazole.

Methods used to derive estimates of effectiveness
Additional data were collected from discussions with physicians who manage onychomycosis.

Estimates of effectiveness and key assumptions
These were not explicitly reported.

Measure of benefits used in the economic analysis
The mycologic cure rate and the number of expected symptom-free days (SFDs) were used as the measure of benefits.
Direct costs
The authors did not report whether or not direct costs were discounted, although the time frame of the study was 3
years. Quantities and costs were reported separately. Direct costs covered drug acquisition costs, the cost of medical
management, and the cost of managing adverse effects. The quantity/cost boundary adopted was that of the third party
payer. The estimation of quantities and costs was based on actual data. Drug costs were based on average wholesale
prices. The cost of medical management was arrived at following meetings with health care professionals who treat

Statistical analysis of costs
A statistical analysis of costs was not carried out.

Indirect Costs
Not included.

Currency
US dollars ($).

Sensitivity analysis
Sensitivity analyses were conducted on key parameters, varied over relevant ranges.

Estimated benefits used in the economic analysis
The mycologic cure rate was 0.411 with griseofulvin, 0.655 with itraconazole (continuous), 0.711 with itraconazole
(pulse), 0.772 with terbinafine, and 0.656 with fluconazole.

The expected number of symptom free days was 456 with griseofulvin, 940 with itraconazole (continuous), 959 with
itraconazole (pulse), 963 with terbinafine, and 695 with fluconazole.

Cost results
Total costs amounted to $2,020.74 with griseofulvin, $1,357.04 with itraconazole (continuous), $762.12 with
itraconazole (pulse), $804.66 with terbinafine, and $950.68 with fluconazole.

Synthesis of costs and benefits
The cost per mycologic cure rate was $4,916.6 with griseofulvin, $2,071.8 with itraconazole (continuous), $1,071.9
with itraconazole (pulse), $1,042.3 with terbinafine, and $1,449.2 with fluconazole.

The expected cost per expected SFD was $6.18 with griseofulvin, $2.34 with itraconazole (continuous), $1.21 with
itraconazole (pulse), $1.23 with terbinafine, and $1.94 with fluconazole.

The rank order of itraconazole (pulse) and terbinafine therapies reversed with minor changes to efficacy rate
parameters, suggesting that the two regimens were equivalent. The rank order of itraconazole (pulse) and terbinafine
would reverse if the mycologic cure rate of itraconazole (pulse) were to decrease to less than 69.5% or if the mycologic
cure rate of terbinafine were to exceed 78.1%.

Authors' conclusions
The two most cost-effective regimens for the treatment of dermatophyte toenail onychomycosis are itraconazole (pulse)
and terbinafine; the least cost-effective comparator is griseofulvin, despite the fact that it has the cheapest drug
acquisition cost per tablet.
CRD COMMENTARY - Selection of comparators
A justification was given for the comparator used (griseofulvin). You, as a user of this database, should decide if these health technologies are relevant to your setting.

Validity of estimate of measure of benefit
The authors did not explicitly state that a systematic review of the literature had been undertaken. However, the methods and conduct of the review were reported in detail. Effectiveness estimates were derived credibly from primary studies and were combined using meta-analysis. Estimation of benefits was obtained directly from the effectiveness analysis.

Validity of estimate of costs
All categories of costs relevant to the perspective adopted were included in the analysis. No indirect costs or costs related to lost productivity were considered, and neither was their importance to the analysis discussed by the authors. Quantities and costs were reported separately. The price year was reported. Sensitivity analyses were conducted on efficacy parameters, but not on quantities or costs.

Other issues
The authors made appropriate comparisons of their findings with those from other studies, but did not address the issue of generalisability to other settings. The authors did not present their results selectively. The study considered patients with toenail onychomycosis and this was reflected in the authors' conclusions. Symptom-free days were used as the measure of benefit instead of quality-of-life measures. The present analysis only focused on dermatophytes as causes of onychomycosis. Other agents such as non-dermaphyte moulds and Candida species were not considered.

Implications of the study
The two most cost-effective regimens for the treatment of dermatophyte toenail onychomycosis are itraconazole (pulse) and terbinafine.

Source of funding
None stated.

Bibliographic details
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Other publications of related interest


Indexing Status
Subject indexing assigned by NLM

MeSH
Administration, Oral; Antifungal Agents /therapeutic use; Cost-Benefit Analysis; Drug Costs /statistics & numerical