The cost-effectiveness and cost of treatment failures associated with systemic psoriasis therapies


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
The study compared the following 12-week treatment regimens for psoriasis:

- psoralen plus ultraviolet (UV) A phototherapy (PUVA), with 40 mg methoxsalen per treatment for 36 treatments;
- narrowband UVB phototherapy (nUVB), 36 treatments;
- acitretin, 25 mg/day;
- cyclosporine, 5 mg/kg per day;
- methotrexate, 15 mg each week;
- alefacept, 15 mg intramuscular (IM) injections, 12 injections;
- efalizumab, 1 mg/kg subcutaneously (SC) each week (consumes a 125-mg vial per injection);
- etanercept, 50 mg SC twice weekly; and
- infliximab, three infusions of 5 mg/kg.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
As this was a modelling study, a hypothetical patient with psoriasis weighing 80 kg was used. Patients suffering from psoriatic arthritis were excluded from the study, as were patients who received multiple systemic agents and not one of the agents under study as monotherapy.

Setting
The setting was not explicitly reported. The economic study was carried out in the USA.

Dates to which data relate
The authors conducted a review of the literature between 1 January 1998 and 1 January 2004. The effectiveness evidence was derived from studies published between 1989 and 2003. The cost data were derived from official sources published in 2003 and were reported for the same price year.
Source of effectiveness data
The effectiveness data were derived from a review and synthesis of completed studies.

Modelling
The authors reported that they constructed a model to evaluate the cost-effectiveness of the treatment options, accounting for the cost of treatment failures. The time horizon appears to have been a 12-week treatment period. No further details of the model were provided in the current study.

Outcomes assessed in the review
The input parameter of the model was not reported in detail, but was defined as the efficacy of the treatment options. In the case of systemic agents, treatment efficacy was defined as the percentage of patients achieving a Psoriasis Area and Severity Index (PASI) of 75% (PASI 75) after 12 weeks of therapy. In the case of phototherapy, treatment efficacy was defined as whole-body clearance after 12 weeks of phototherapy.

Study designs and other criteria for inclusion in the review
Completed randomised controlled trials (RCTs) that had been written in English and published in peer-reviewed journals were included in the review. Only studies that involved at least one of the therapeutic agents under study were eligible for inclusion. Studies that referred to patients with psoriatic arthritis, or studies where the therapeutic agents were used only in topical applications, were excluded from the review. The agents under study should have been used as systematic treatments, and patients in the studies included in the review should have followed monotherapy. In addition, only studies that assessed treatment efficacy as PASI 75% improvement after 12 weeks of treatment with systemic agents, or that determined total body clearance after roughly 12 weeks of phototherapy, were included. The duration of treatment in the included studies ranged from 10 to 14 weeks. In terms of the dosages, the review only included studies in which administration of alefacept was IM, etanercept was provided at a dose of 50 mg SC twice a week, infliximab at a dose of 5 mg/kg, phototherapy was administered three times weekly, and psoralen was administered orally.

Sources searched to identify primary studies
PubMed (National Library of Medicine) was searched to identify primary studies.

Criteria used to ensure the validity of primary studies
No specific criteria were used to ensure the validity of the primary studies.

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

Number of primary studies included
Overall, 13 RCTs that met the inclusion and exclusion criteria were included in the review and used as sources of effectiveness evidence.

Methods of combining primary studies
The authors reported that if more than one study on the same agent was identified, the weighted average of the efficacies was used depending on the number of patients under the treatment module.

Investigation of differences between primary studies
The authors investigated differences between the primary studies, especially in terms of the patients' demographics, but
no results from statistical tests of homogeneity were reported.

**Results of the review**
The weighted average efficacy was 52% for acitretin, 21% for alefacept, 82% for cyclosporine, 25% for efalizumab, 49% for etanercept, 82% for infliximab, 70% for methotrexate, 72% for nUVB and 84% for PUVA.

**Measure of benefits used in the economic analysis**
The authors used the percentage of patients achieving PASI 75 or whole-body clearance (treatment efficacy) and treatment failures per single patient's success as measures of benefit in the economic analysis. These were derived directly from the model.

**Direct costs**
The direct health services costs used in the analysis were:

- level 3 return follow-up evaluation/management outpatient visits to physician;
- level 1 evaluation/management nursing outpatient visits;
- the cost of laboratory tests (complete blood count with differential, complete metabolic profile, lipid panel, liver function profile, magnesium level, T-cell CD4 count);
- the cost of chest X-ray and tuberculosis skin test;
- the cost of PUVA treatment;
- the cost of liver biopsy (including day hospital costs); and
- the costs of 1 hour of infusion and each additional hour of infusion.

It was reported that the costs of adverse events due to treatment agents were not included in the analysis. The costs and the quantities were reported separately. The cost data were derived from official published sources (mostly Medicare median reimbursement) and were reported for the price year 2003. Discounting was not necessary since the costs were incurred during less than 2 years.

**Statistical analysis of costs**
The costs were treated deterministically.

**Indirect Costs**
The indirect costs were not included in the analysis.

**Currency**
US dollars ($).

**Sensitivity analysis**
The authors conducted a one-way sensitivity analysis to investigate the robustness of the results to variability in the data. Since it was not possible to estimate 95% confidence intervals or to conduct a full meta-analysis, the efficacy estimates for the therapeutic agents were varied by +/- 5% in the sensitivity analysis.
Estimated benefits used in the economic analysis
See the 'Results of the Review' section for treatment efficacy. The number of failed treatments per successful treatment was not reported.

Cost results
The total costs were reported per patient. These were $3,921 for PUVA, $2,658 for nUVB, $436 for methotrexate, $1,419 for acitretin, $2,464 for cyclosporine, $13,393 for alefacept, $4,299 for efalizumab, $7,993 for etanercept and $8,774 for infliximab.

Synthesis of costs and benefits
The cost per 1% of patients achieving PASI 75 or whole-body clearance was $623 for methotrexate, $2,729 for acitretin, $2,969 for cyclosporine, $3,692 for nUVB, $4,668 for PUVA, $10,700 for infliximab, $16,312 for etanercept, $17,196 for efalizumab and $63,776 for alefacept.

The cost of treating failures per single patient success was $187 for methotrexate, $1,310 for acitretin, $505 for cyclosporine, $1,034 for nUVB, $767 for PUVA, $1,926 for infliximab, $8,319 for etanercept, $12,897 for efalizumab and $50,383 for alefacept.

The incremental cost-effectiveness analysis demonstrated that methotrexate was the least costly and more effective option, while cyclosporine demonstrated greater efficacy at an additional cost of $153 per additional 1% of patients achieving PASI 75 or whole-body clearance end point. PUVA demonstrated a greater efficacy than cyclosporine at an additional cost of $1,457 per additional 1% of patients achieving PASI 75 or whole-body clearance.

Authors' conclusions
Methotrexate would appear to be the most cost-effective agent for treating severe psoriasis. Greater efficacy can be achieved with cyclosporine and phototherapy (psoralen plus ultraviolet A phototherapy, PUVA), although at a greater cost. "Because of the high cost of treatment failures, access to a wide array of therapies and combination regimens should not be discouraged by physicians or insurers."

CRD COMMENTARY - Selection of comparators
The comparators chosen would appear to represent the most commonly used therapeutic options in the authors' setting. You should decide if these represent widely used technologies in your own setting.

Validity of estimate of measure of effectiveness
The authors described the systematic identification, selection and synthesis of evidence to form an estimate of effectiveness. The methodological conduct of the review was satisfactory. Estimates of effectiveness used weighted averages to reflect differences in sample sizes.

Validity of estimate of measure of benefit
The measures of benefit used in the economic analysis were the percentage of patients achieving PASI 75 or whole-body clearance (efficacy of treatment) and treatment failures per single patient's success. These were derived directly from the model.

Validity of estimate of costs
Although the perspective adopted in the economic analysis was not reported, it was not societal since the indirect costs were not included in the analysis. The costs of adverse events of treatment agents were not included, and it is not known how far their omission has affected the authors' conclusions. The costs and the quantities were reported separately, thus enhancing the reproducibility of the study in other settings. The costs were treated deterministically and no sensitivity
analysis on the costs or quantities of resources used was performed. This may limit the interpretation of the study findings. For example, the case of some managed care organisations that receive discount on products (e.g. treatment agents) was not reflected in the analysis. Discounting was not necessary given the short time horizon of the study. The price year was reported, which will aid any future reflation exercises.

Other issues
The authors did not compare their findings with those from other studies, although this might have been because of the lack of published studies incorporating treatment failure in their analysis. The issue of generalisability of the results to other settings was not directly addressed. The authors do not appear to have presented their results selectively and the scope of the analysis was reflected in their conclusions.

The authors reported several limitations to their study. First, the efficacy estimates were only derived from RCTs with a limited time horizon of 12 weeks, thus the long-term effects of treatment were not accounted for in the analysis. Second, PASI 75 improvement, which was used as an efficacy measure in all studies included in the review, comprises only a proxy measure that might not reflect "real-world" efficacy. The authors reported that there was disparity in mean PASI scores in patients before starting up the treatment, which would makes across-study comparisons difficult. Third, the analysis did not include combination regimens which are commonly used in clinical practice. Finally, the analysis did not consider the costs of adverse events of the therapies, or other associated expenses, to the patients.

Implications of the study
The authors did not make explicit recommendations for changes in policy or practice. They called for future research on the cost-effectiveness of combination psoriasis treatment regimens. In addition, the discussion highlighted areas where more information is necessary.

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