Strategy to manage the treatment of severe psoriasis: considerations of efficacy, safety and cost


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 examined several interventions for the treatment of severe psoriasis:

- ultraviolet light Type B (UVB);
- psoralen plus ultraviolet light (PUVA);
- methotrexate, 10, 15 or 20 mg/week;
- acitretin, 25 mg/day;
- cyclosporin, 240 or 400 mg/day; and
- three new biological treatments, etanercept (25 or 50 mg, twice weekly), infliximab 5 mg/kg or 10 mg/kg (six infusions per year of, respectively, 400 mg or 800 mg) and alefacept 7.5 mg (18 infusions per year) or 15 mg (18 injections per year).

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised a hypothetical cohort of patients suffering from severe psoriasis.

Setting
The setting was primary and secondary care. The economic study was carried out in the USA.

Dates to which data relate
The effectiveness data were derived from studies published between 2000 and 2003. No dates were explicitly reported for the resource use data, which were mainly based on expert opinion. The price year was 2002.

Source of effectiveness data
The effectiveness evidence was derived from a synthesis of completed studies and experts' opinions.

Outcomes assessed in the review
The outcome estimated from the literature was treatment efficacy. This was defined in accordance with the Psoriasis Area and Severity Index (PASI) clearance criterion of 75%.

**Study designs and other criteria for inclusion in the review**
The authors stated that a review of the literature was undertaken to identify relevant primary studies. However, no information about the review was reported. It was stated that few, if any, randomised controlled trials comparing the different treatments were available.

**Sources searched to identify primary studies**
Not reported.

**Criteria used to ensure the validity of primary studies**
Not reported.

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

**Number of primary studies included**
Five primary studies provided clinical data.

**Methods of combining primary studies**
Not reported.

**Investigation of differences between primary studies**
Not reported.

**Results of the review**
The treatment efficacy was 70% with UVB, 80% with PUVA, 30% with methotrexate, 30% with acitretin, 70% with cyclosporin, 47% with etanercept, 80% with infliximab and 40% with alefacept.

**Methods used to derive estimates of effectiveness**
The authors stated that some experts’ opinions were used to derive clinical data.

**Estimates of effectiveness and key assumptions**
The precise role played by expert opinion was unclear. Conservative estimates were used for methotrexate.

**Measure of benefits used in the economic analysis**
The summary benefit measure was treatment success (efficacy). This was estimated from the review of the literature.

**Direct costs**
The cost analysis appears to have been carried out from the perspective of a third-party payer. The health service costs included were for drugs, office visits, laboratory tests, radiological studies, procedures and infusions. The costs of rare events, such as hospitalisation for liver transplantation, were excluded. A detailed breakdown of the cost items was
reported. The unit costs were presented separately from the quantities of resources used. The resource use data were mainly derived from authors' assumptions and clinical guidelines. The costs were estimated from the Medicare fee schedule and average wholesale prices. Discounting was not relevant as the costs for one year were estimated. The price year was 2002.

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

**Indirect Costs**
The indirect costs do not appear to have been included in the economic evaluation.

**Currency**
US dollars ($).

**Sensitivity analysis**
A univariate sensitivity analysis was performed to assess the robustness of the cost-effectiveness estimates to variations in the efficacy rates. The alternative ranges of values were derived from the literature.

**Estimated benefits used in the economic analysis**
The treatment efficacy was 70% with UVB, 80% with PUVA, 30% with methotrexate, 30% with acitretin, 70% with cyclosporin, 47% with etanercept, 80% with infliximab and 40% with alefacept.

**Cost results**
The annual costs ranged from $1,600 to $34,600.

Methotrexate was the least costly therapy ($1,600), followed by UVB ($3,600) and PUVA ($4,600).

Acitretin was slightly less costly than cyclosporin ($5,200 versus $6,500 to $10,000 for 3 to 5 mg/kg per day).

The annual cost of alefacept ranged from $16,000 to $20,000 (uncertainty was due to its intermittent use).

The annual cost of etanercept ranged from $16,900 (25 mg twice weekly) to $33,000 (50 mg twice weekly).

The annual cost of infliximab was approximately $18,000 (5 mg/kg).

**Synthesis of costs and benefits**
Average cost-effectiveness ratios were calculated to combine the costs and benefits of the alternative treatments for severe psoriasis.

The average cost per treatment success was $5,400 with methotrexate, $5,100 with UVB, $5,700 with PUVA, $14,200 with cyclosporin, $17,300 with acitretin, $35,900 with etanercept, $40,600 with alefacept and $22,500 with infliximab.

The authors acknowledged that, owing to the limitations of the available evidence, these cost-effectiveness ratios should be considered as rough estimates.

The sensitivity analysis showed that:

methotrexate remained the most cost-effective strategy;
UVB and PUVA had comparable cost-effectiveness ratios; the cost-effectiveness of cyclosporin was higher than that of phototherapy, but lower than that of biological agents; and acitretin and infliximab had similar cost-effectiveness ratios.

In general, biological agents had higher (average) cost-effectiveness ratios than the other treatments.

Authors' conclusions
Ultraviolet light Type B (UVB) could be considered the most cost-effective first-line treatment for severe psoriasis. The choice of the second-line therapy might be between methotrexate, psoralen plus ultraviolet light (PUVA), alefacept, etanercept and infliximab, depending on cost issues and their long-term safety profile.

CRD COMMENTARY - Selection of comparators
The authors justified the choice of the comparators that were examined in the study. All possible treatments available for severe psoriasis were presented, and the advantages and disadvantages of each approach highlighted. Some therapies were then excluded and the reasons for their exclusion expanded. Thus, eight comparators considered in the study were appropriately chosen. Dosages were also reported. You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness evidence came from published studies. However, the methods and conduct of the review were not reported. No information on the design and characteristics of the primary studies was provided, thus it was not possible to assess the validity of the primary estimates. The authors stated that the efficacy estimates were not based on comparative studies, which represents a strong limitation of the study. Also, it was stated that few, if any, randomised controlled trials were available. Experts' opinions were also used, but to what extent these opinions affected the primary estimates was unclear. Sensitivity analyses were performed to assess the robustness of the final cost-effectiveness estimates to variations in the clinical data.

Validity of estimate of measure of benefit
The summary benefit measure was specific to the disease considered in the study and would not be comparable with the benefits of other health care interventions. Further, the authors stated that psoriasis has a great impact on quality of life, but the use of treatment success as a benefit measure does not capture this aspect of health. The use of a more generalisable measure incorporating quality of life aspects, such as quality-adjusted life-years, would have been helpful.

Validity of estimate of costs
The perspective adopted in the study was unclear as the authors stated that both the direct and indirect costs would have been included. In fact, only the direct medical costs were actually considered. Thus, the perspective appears to have been that of a third-party payer. Extensive information on the unit costs and sources of data was provided, which enhances the possibility of replicating the cost analysis in other settings. Resource use was mainly based on opinions. The authors stated that resource consumption did not reflect actual drug doses or the use of health care services. In fact, the cost calculation was hypothetical and might not be representative of actual expenditures for payers. The cost estimates were treated deterministically and were specific to the study setting. The price year was reported, which will facilitate reflation exercises in other time periods. The authors noted difficulties with the assessment of costs, owing to the intermittent nature of some treatments or dosage titration for other agents.

Other issues
The authors did not make extensive comparisons of their findings with those from other studies. They also did not address the issue of the generalisability of the study results to other settings. Limited sensitivity analyses were
performed and the overall external validity of the study was low. Average rather than incremental cost-effectiveness ratios were used, and this represents a weakness of the study. The time horizon of the study appears to have been very short and some categories of costs, potentially relevant in the long term, were excluded. In general, the main limitation of the study appears to have been the availability of poor clinical data, as the authors acknowledged. The study referred to patients with severe psoriasis and this was reflected in the authors’ conclusions.

Implications of the study
The study results highlighted the difficulties of choosing the most appropriate treatment for severe psoriasis. Incentives favouring the use of UVB should be maintained in order to use it as the first-line treatment for psoriasis.

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