New treatments for psoriasis: which biologic is best?  

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  
This study considered biological treatments for psoriasis. The treatments studied were:

- alefacept, 15 mg intramuscularly once a week;
- efalizumab, 1 mg/kg subcutaneously once a week and 2 mg/kg subcutaneously once a week;
- etanercept, 25 mg subcutaneously once a week and 25 mg subcutaneously twice a week;
- etanercept, 50 mg subcutaneously twice a week for 12 weeks followed by 50 mg subcutaneously once a week;
- infliximab, 3, 5 and 10 mg/kg intravenously (three infusions);
- adalimumab, 40 mg subcutaneously once a week and 40 mg subcutaneously every other week.

Type of intervention  
Treatment.

Economic study type  
Cost-effectiveness analysis.

Study population  
The study population comprised patients with moderate to severe psoriasis. No inclusion or exclusion criteria were reported.

Setting  
The setting was tertiary care. The economic study was carried out in the USA.

Dates to which data relate  
The clinical effectiveness data were taken from studies published between 2001 and 2005. The price year was 2004.

Source of effectiveness data  
The effectiveness data were derived from a review or synthesis of published studies.

Outcomes assessed in the review  
The review identified the percentage of patients achieving a 75% improvement in their Psoriasis Area and Severity Index (PASI) and the mean improvement in the Dermatology Life Quality Index (DLQI).
Study designs and other criteria for inclusion in the review
Only data from randomised controlled trials were included in the review.

Sources searched to identify primary studies
PubMed was searched for primary studies.

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
The data were taken from a total of 16 published sources.

Methods of combining primary studies
Where data were taken from more than one trial, they were combined using a weighted average based on the sample size.

Investigation of differences between primary studies
Not reported.

Results of the review
The proportions of patients experiencing a 75% improvement in their PSAI with the various medications were as follows:

- aplefacept 15 mg intramuscularly once a week, 21%;
- efalizumab 1 mg/kg subcutaneously once a week, 28%;
- efalizumab 2 mg/kg subcutaneously once a week, 28%;
- etanercept 25 mg subcutaneously once a week, 14%;
- etanercept 25 mg subcutaneously twice a week, 33%;
- etanercept 50 mg subcutaneously twice a week for 12 weeks followed by 50 mg subcutaneously once a week, 49%;
- infliximab 3 mg/kg intravenously (three infusions), 72%;
- infliximab 5 mg/kg intravenously (three infusions), 84%;
- infliximab 10 mg/kg intravenously (three infusions), 73%;
- adalimumab 40 mg subcutaneously every other week, 53%;
- adalimumab 40 mg subcutaneously once a week, 80%.

The mean improvements in DLQI were as follows:
alefacept 15 mg intramuscularly once a week, 4.9;

efalizumab 1 mg/kg subcutaneously once a week, 5.6;

etanercept 25 mg subcutaneously once a week, 5.8;

etanercept 25 mg subcutaneously twice a week, 7.0;

etanercept 50 mg subcutaneously twice a week for 12 weeks followed by 50 mg subcutaneously once a week, 7.5;

infliximab 3 mg/kg intravenously (three infusions), 8.8;

infliximab 5 mg/kg intravenously (three infusions), 10.3.

Measure of benefits used in the economic analysis
The measures of health benefit used were the percentage of people experiencing a 75% improvement in their PASI and the improvement in the DLQI.

Direct costs
The direct costs of the health care payer were identified in this study. Costs borne by the patient, both health care and non-health care, were not included in the analysis. Resource use was estimated using a hypothetical 80-kg patient with drug use, physician visits and laboratory testing estimated by the authors. The unit drug costs were taken from the 2004 Drug Topics Red Book, while the unit costs of physician visits and laboratory tests were taken from the 2004 Medicare fees. The price year was 2004.

Statistical analysis of costs
The cost data were treated deterministically.

Indirect Costs
No indirect costs were included in this study.

Currency
US dollars ($).

Sensitivity analysis
No sensitivity analysis was undertaken.

Estimated benefits used in the economic analysis
See values reported under the ‘Results of the Review’ section.

Cost results
The study identified the total annual cost per patient with the various medications:

alefacept 15 mg intramuscularly once a week, $20,376;

efalizumab 1 mg/kg subcutaneously once a week, $18,214;

efalizumab 2 mg/kg subcutaneously once a week, $36,050;
etanercept 25 mg subcutaneously once a week, $8,849;
etanercept 25 mg subcutaneously twice a week, $17,402;
etanercept 50 mg subcutaneously twice a week for 12 weeks followed by 50 mg subcutaneously once a week, $21,349;
infliximab 3 mg/kg intravenously (three infusions), $123,245;
infliximab 5 mg/kg intravenously (three infusions), $167,395;
infliximab 10 mg/kg intravenously (three infusions), $33,993;
adalimumab 40 mg subcutaneously every other week, $17,402;
adalimumab 40 mg subcutaneously once a week, $34,508.

**Synthesis of costs and benefits**
The study identified the following costs per patient achieving PASI-75:
alefacept 15 mg intramuscularly once a week, $74,625;
efalizumab 1 mg/kg subcutaneously once a week, $18,200;
efalizumab 2 mg/kg subcutaneously once a week, $35,350;
etanercept 25 mg subcutaneously once a week, $20,236;
etanercept 25 mg subcutaneously twice a week, $13,827;
etanercept 50 mg subcutaneously twice a week for 12 weeks followed by 50 mg subcutaneously once a week, $17,600;
infliximab 3 mg/kg intravenously (three infusions), $9,768;
infliximab 5 mg/kg intravenously (three infusions), $10,896;
infliximab 10 mg/kg intravenously (three infusions), $24,662;
adalimumab 40 mg subcutaneously every other week, $8,466;
adalimumab 40 mg subcutaneously once a week, $10,652.
The study identified the following costs per patient achieving a minimally important difference in DLQI:
alefacept 15 mg intramuscularly once a week, $27,136;
efalizumab 1 mg/kg subcutaneously once a week, $5,277;
etanercept 25 mg subcutaneously once a week, $2,109;
etanercept 25 mg subcutaneously twice a week, $3,289;
etanercept 50 mg subcutaneously twice a week for 12 weeks followed by 50 mg subcutaneously once a week, $6,073;
infliximab 3 mg/kg intravenously (three infusions), $5,109.
Authors' conclusions
The authors concluded that no single biologic agent was "best".

CRD COMMENTARY - Selection of comparators
The authors compared five different biologic agents with eleven dosage regimens for the treatment of psoriasis. They appear to have included these treatments as they are the currently available biologic treatments for psoriasis; although it should be noted that not all of the treatments have been approved by the Food and Drug Administration or European Medicines Agency. You should consider how these options compare with usual practice in your own setting prior to applying the results of this study.

Validity of estimate of measure of effectiveness
The measure of effectiveness of the eleven treatment regimens was identified through a review of published studies. The authors did not indicate whether a systematic review had been undertaken, but they did report the source searched to identify studies. They also indicated that only randomised controlled trials were used. Where more than one primary study was identified, the data were combined using weighted averages which took account of the differing sample sizes of the primary studies. The authors did not consider the impact of differences between the primary studies when identifying effectiveness, although they did highlight that the study populations might have varied slightly, and that this should be considered when considering the results presented. In addition, the authors highlighted the limitation of only using a 12-week time horizon for the evaluation of efficacy for psoriasis treatment. A more comprehensive systematic review of the effectiveness literature would have increased the likelihood that the best available evidence had been identified and included in the analysis. However, as the authors searched only one database, it is not possible, in this instance, to ascertain whether this was the case.

Validity of estimate of measure of benefit
The measures of health benefit used in the economic analysis were taken directly from the review. The authors combined the cost data with two measures of health benefit. The use of a dermatology-related measure of health utility (the DLQI) will allow the results of this study to be directly compared with other dermatology treatments.

Validity of estimate of costs
The study appears to have been carried out from the perspective of a health care payer. However, no costs associated with adverse events were included, which means it is likely that the study underestimated the costs associated with these regimens. Some unit drug costs were provided in the paper, but a complete breakdown of resource use and unit costs was not provided. No statistical or sensitivity analyses of the cost data were performed. This means that the level of uncertainty around the cost data was not explored. These factors limit the generalisability of the study findings. A clear price year was reported, which will facilitate future reflation exercises.

Other issues
The authors do not appear to have presented their results selectively, but they did not draw any clear conclusions from their analysis. They did not compare their results with those from other studies and did not consider how their findings could be generalised to other settings. In addition, the authors highlighted the fact that a lack of trials comparing these biologic agents head-to-head limits the confidence in the results that have been obtained.

Implications of the study
The authors did not make any recommendations for further research or changes to practice, although they did acknowledge the importance of educating patients prior to treatment, thus allowing informed patient preferences to be incorporated into any decision-making process.

Source of funding
NHS Economic Evaluation Database (NHS EED)
Produced by the Centre for Reviews and Dissemination
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Bibliographic details

PubMedID
16766334

DOI
10.1080/09546630600552273

Indexing Status
Subject indexing assigned by NLM

MeSH
Adalimumab; Antibodies, Monoclonal /administration & dosage /economics /therapeutic use; Antibodies, Monoclonal, Humanized; Cost-Benefit Analysis; Dermatologic Agents /administration & dosage /economics /therapeutic use; Etanercept; Humans; Immunoglobulin G /administration & dosage /economics /therapeutic use; Immunologic Factors /administration & dosage /economics /therapeutic use; Infliximab; Injections; Psoriasis /drug therapy /pathology; Receptors, Tumor Necrosis Factor /administration & dosage /therapeutic use; Recombinant Fusion Proteins /administration & dosage /economics /therapeutic use; United States

AccessionNumber
22006000952

Date bibliographic record published
30/11/2006

Date abstract record published
30/11/2006