Cost-effectiveness of tacrolimus ointment in adults and children with moderate and severe atopic dermatitis: twice-weekly maintenance treatment vs. standard twice-daily reactive treatment of exacerbations from a third party payer (UK National Health Service) perspective

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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.

CRD summary
This study investigated the cost-effectiveness of tacrolimus ointment as twice-weekly maintenance treatment versus as standard reactive treatment, for moderate or severe atopic dermatitis. The authors concluded that maintenance therapy was cost-effective, because it provided additional health benefits, at a lower cost, compared with reactive therapy. The methods were mostly reasonable and transparent, but it is not clear how certain the results are due to a lack of uncertainty statistics.

Type of economic evaluation
Cost-utility analysis

Study objective
The aim was to examine the costs and health outcomes of tacrolimus ointment for adults and children with moderate or severe atopic dermatitis.

Interventions
Tacrolimus ointment as twice-weekly maintenance treatment was compared with the standard reactive treatment of moderate or severe atopic dermatitis. The dose of tacrolimus ointment was 0.1% for adults and 0.03% for children. Standard reactive treatment was usage when a disease exacerbation occurred.

Location/setting
UK/primary care.

Methods
Analytical approach:
A decision-analytic model was used to synthesise the data from key published studies and epidemiology reports. These data were primarily from the Clinical Study on Tacrolimus Ointment Over the Long-Term (CONTROL Study; Thaci, et al. 2008 and Wollenberg, et al. 2008, see ‘Other Publications of Related Interest’ below for bibliographic details). The time horizon was 12 months and the authors stated that they took a UK NHS perspective.

Effectiveness data:
The key clinical outcomes were the days in disease exacerbation, the discontinuation rate, and the time until discontinuation. These data were from the CONTROL Study for maintenance treatment, manufacturer trial reports (Data on file at Astellas Pharma Europe R&D. Study references FG-506-06-40 and FG506-06-41, 2007), and a relevant publication (Zuberbier, et al. 2006, see ‘Other Publications of Related Interest’ below for bibliographic details) that included patients with moderate-to-severe atopic dermatitis. Adverse events were assumed to be equivalent for the two strategies.

Monetary benefit and utility valuations:
Utility data were used to adjust the survival days and applied to the period of disease exacerbation. These values were from the adult participants in the CONTROL Study and a 2005 published health technology assessment for children.
Measure of benefit:
The measure of benefit was quality-adjusted life-years (QALYs).

Cost data:
The direct medical costs included the tacrolimus ointment, consultant dermatology and out-patient visits, phototherapy, topical steroids, oral medications, and in-patient stays. Published sources were used to measure and value these resources. These included MIMS 2009, NHS National Reference Costs, and the Personal Social Services Research Unit 2008. The costs of discontinuing tacrolimus were from 16 clinical experts. Costs were reported in UK pounds sterling (£).

Analysis of uncertainty:
The model parameters were examined in one-way and probabilistic sensitivity analyses. The one-way analyses on all parameters used ranges of values that were the 95% confidence interval limits in the literature. The results were reported in a table and the text.

Results
Over 12 months, for adults with moderate atopic dermatitis, the total costs were £733.94 for maintenance treatment and £902.02 for standard treatment. The QALYs were 0.86 for maintenance treatment and 0.85 for standard treatment. Savings in the costs of discontinuation in the maintenance arm completely offset the extra costs of tacrolimus ointment. Similar results were found adults with severe atopic dermatitis.

The cost savings were £168.08 for moderate and £932.89 for severe adult atopic dermatitis. The incremental QALYs gained were 0.01 for moderate and 0.05 for severe adult atopic dermatitis. Tacrolimus ointment maintenance was dominant as it was more effective and cost saving compared with standard treatment, for both moderate and severe disease.

Similar results were found for children; tacrolimus ointment maintenance was dominant.

Maintenance treatment was dominant in all the one-way sensitivity analyses, except for the time to discontinuation in children with severe atopic dermatitis. Maintenance treatment in adults was cost-effective in 67%, for moderate disease, and 88%, for severe disease, of probabilistic simulations at the acceptability threshold of £30,000 per QALY.

Authors' conclusions
The authors concluded that maintenance therapy, using tacrolimus ointment, for children and adults with moderate or severe atopic dermatitis, produced additional health benefits, at lower costs, and was cost-effective, compared with reactive treatment.

CRD commentary
Interventions:
The two strategies were well described. It was unclear why topical corticosteroids and topical calcineurin inhibitors were not analysed, given the 12-month time horizon.

Effectiveness/benefits:
The clinical trials were not described, but they were referenced and should have been reviewed during the European tacrolimus application. No uncertainty statistics were presented for the clinical data. The utility values were elicited from adults and children with atopic dermatitis flares and the results were published; the measurement tool was not reported. The source studies should be consulted to assess the internal validity of these utilities.

Costs:
The price year was not reported. The resource usage was based on expert opinion and is uncertain. The authors reported that the discontinuation costs were conservative towards maintenance therapy. The assumptions and estimates were reported and can be checked. The unit costs were from publicly available sources.

Analysis and results:
The authors discussed their findings, compared with those of other pharmacoeconomic studies, which had similar findings. The results of the one-way sensitivity analyses were not fully reported, making it impossible to assess the impact of changes in the key variables. No uncertainty statistics for the data inputs were reported and it was not clear where the sensitivity analysis ranges were from. It would have been better to have used patient-level resource data from the CONTROL Study, providing actual resource use.

Concluding remarks:
The methods were mostly reasonable and transparent, but it is not clear how certain the results are due to a lack of uncertainty statistics.

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