Value-based medicine, comparative effectiveness, and cost-effectiveness analysis of topical cyclosporine for the treatment of dry eye syndrome

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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 examined the cost-effectiveness of topical 0.05% cyclosporine emulsion therapy compared with the vehicle for cyclosporine, for the management of patients with moderate-to-severe dry eye syndrome that had not responded to conventional therapy. The authors concluded that the 0.05% cyclosporine emulsion was cost-effective. The methodology was sound, but more detailed reporting of the sources of the clinical inputs would have been useful. The authors' conclusions appear to be valid.

Type of economic evaluation
Cost-utility analysis

Study objective
The objective was to compare two options for the management of patients, with moderate-to-severe dry eye syndrome that had not responded to conventional lubricant therapy.

Interventions
The interventions were 0.05% cyclosporine ophthalmic emulsion (Restasis; Allergan Inc, Irvine, California) twice per day, and the vehicle for cyclosporine ophthalmic emulsion twice per day (placebo). These were also compared with no treatment.

Location/setting
USA/primary care.

Methods
Analytical approach:
The costs and benefits were from a variety of published sources and they were synthesised using simple mathematical equations. The time horizon appears to have been six months. The authors reported that the base case took a third-party payer perspective and a societal perspective was considered in a sensitivity analysis.

Effectiveness data:
The clinical data for topical cyclosporine 0.05% emulsion were from four multi-centre, randomised controlled trials (RCTs) and other published studies. Two of the multi-centre trials were submitted by Allergan, to the Food and Drug Administration (FDA). The time trade-off utilities for visual acuity and adverse events were from the literature and they were obtained with the approval of the Wills Eye Hospital institutional review board. The effectiveness was measured by the utilities, which were dependent on vision and other factors from the composite score of symptom severity. The main clinical effect parameters were the utilities.

Monetary benefit and utility valuations:
The utility values were from published sources and the patients’ utilities were assessed using the time trade-off technique.

Measure of benefit:
Quality-adjusted life-years (QALYs) were the measure of benefit.
Cost data:
The costs included those of the intervention and physician visits, including those for treatment-related adverse events. For the societal perspective, reduced productivity due to dry eyes was also included. The unit costs and resource quantities were reported separately. The costs were from official sources or from the literature. They were reported in US dollars ($) for the price year 2007.

Analysis of uncertainty:
The parameter uncertainty was investigated, using one-way sensitivity analysis. The parameters varied included the discount rate, the annual cost of 0.05% cyclosporine, the QALYs gained due to the intervention, and the percentage of people able to work at full productivity due to the intervention. Scenarios including and excluding all adverse events were also reported.

Results
In the base case, compared with no treatment, the expected QALY gain at one year was 0.0534 with cyclosporine topical emulsion and 0.0215 with the vehicle. From the third-party payer perspective, the total cost of cyclosporine emulsion was $1,834 and the total cost of the vehicle was $648. The incremental cost of cyclosporine over the vehicle was $1,186.

The incremental cost-effectiveness ratio (ICER) of cyclosporine emulsion compared with the vehicle was $37,179 per QALY. From a societal perspective, the ICER of cyclosporine emulsion compared with the vehicle was $34,953 per QALY.

The sensitivity analysis demonstrated that these results were robust.

Authors' conclusions
The authors concluded that 0.05% ophthalmic cyclosporine emulsion was a cost-effective intervention for the management of patients, with moderate-to-severe dry eye syndrome that had not responded to conventional lubricant therapy.

CRD commentary
Interventions:
The rationale for the choice of comparators was explicit and the usual treatment in the authors’ setting was included. Alternative treatments were not discussed and, if they were available, only a partial analysis was conducted.

Effectiveness/benefits:
No systematic review of the literature was reported and the authors appear to have selected the sources of effectiveness data. This makes it impossible to be sure that the best available evidence was used. In general, RCTs are valid sources for effectiveness data, given the strengths of their design, but the details of the randomisation procedures, power calculations to ensure an adequate sample size, and the methods of analysis, were not reported. This means that it is not possible to objectively assess the validity of these trials, but their references were reported and could be consulted. The derivation of the benefit measure was reported and a validated instrument was used. QALYs were an appropriate measure because they not only synthesise the quality and quantity of life, but also allow cross-disease comparisons.

Costs:
The costs reflected the perspective adopted. The sources of unit costs, the quantities of resource use, and the unit costs were reported, enhancing the transparency of the analysis. Some costs were omitted from the analysis, but these were explicitly reported; it is unclear whether their omission affected the conclusions. Adjustments for inflation and the price year were reported, facilitating future reflation exercises. Overall, the costing appears to have been well conducted and reported.

Analysis and results:
The costs and benefits were appropriately synthesised, using an incremental approach. The issue of uncertainty was partially addressed, using a deterministic approach, for specific parameters. A probabilistic analysis would have strengthened the conclusions and better assessed the uncertainty. The authors highlighted the main limitations and fully
discussed their sensitivity analysis.

**Concluding remarks:**
The methodology was sound, but more detailed reporting of the sources of the clinical inputs would have been useful. The authors’ conclusions appear to be valid.

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