Drug pricing for a novel treatment for wet macular degeneration: using incremental cost-effectiveness ratios to ensure societal value
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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.

Health technology
Two strategies for the treatment of wet age-related macular degeneration (AMD) were compared. Standard treatment consisted of photodynamic therapy (PDT) using verteporfin (Visudyne), while the investigational treatment consisted of juxtascleral administration of anecortave acetate (Retaane; 15 mg for depot suspension).

Type of intervention
Treatment.

Economic study type
Cost-utility analysis.

Study population
The characteristics of the target population were not discussed in the current modelling study. The authors only mentioned that a hypothetical cohort of patients with AMD was used with similar characteristics to the one used in Phase III of the clinical trial conducted to assess the safety and efficacy of anecortave acetate.

Setting
As this was a modelling study, a setting was not explicitly stated. The economic study was carried out in the USA.

Dates to which data relate
The effectiveness evidence was derived from an ongoing clinical trial, the dates of which were not reported. In addition, data were derived from a meeting of the American Academy of Ophthalmology held in 2004. The cost data were derived from published Medicare data, but the related date was not reported. Additional cost data were derived from other sources published between 1989 and 2005 and from personal communication with experts. The price year was not explicitly reported.

Source of effectiveness data
The effectiveness data were derived from Phase III of an ongoing clinical trial and from data presented in a meeting of the American Academy of Ophthalmology which were mainly assessed electronically.

Modelling
The authors constructed various cost-utility models to compare the two treatment options. Four scenarios for the incremental cost-effectiveness ratio (ICER) threshold were investigated: $100,000, $50,000, $20,000 and $0 per QALY. The patients were classified into one of 6 categories based on distance acuity from the better-seeing eye: better than 20/32 (category I),
20/32 to better than 20/50 (category II),
20/50 to better than 20/80 (category III),
20/80 to better than 20/150 (category IV),
20/150 to better than 20/250 (category V), and
20/250 vision or worse (category VI).

For each category of patient, three health states were assessed. These were three-line improvement, stable and three-line loss. The time horizon of the models was one year. The reference-case scenario assumed that those who received PDT would receive 3.1 treatments in the 1-year period. Further details of the model were not reported.

Outcomes assessed in the review
The input parameters used in the model were the probabilities of maintained vision, three-line loss and three-line improvement in all patients who received anecortave, who received anecortave and were retreated within 182 days without reflux, and who received PDT. Maintained vision was defined as less than a 3-line loss in logarithm of minimum angle of resolution visual acuity.

Study designs and other criteria for inclusion in the review
Event probabilities were derived from a randomised clinical trial that compared the safety and efficacy of anecortave administration to PDT with verteporfin. Treatment efficacy was derived from proprietary data provided by Alcon Research Ltd. (Forth Worth).

Sources searched to identify primary studies
No further sources were searched to identify the 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
Overall, data from two studies were included in the review.

Methods of combining primary studies
The authors used a Delphi panel to obtain the vision-stratified rates of falls and depression.

Investigation of differences between primary studies
The authors do not appear to have investigated differences between the primary studies.

Results of the review
The probability of visual stabilisation was:

45% in all patients who received anecortave;
57% in patients who received anecortave and were treated within 182 days without reflux; and

49% in patients treated with PDT.

The probability of visual loss was:

55% in all patients who received anecortave;

43% in patients who received anecortave and were treated within 182 days without reflux; and

51% in patients who received PDT.

The authors noted that patients with no reflux at the time of retreatment, and who received their second injection within 182 days after their first injection, had a higher probability of achieving visual stability after one year in comparison with patients with reflux (50% versus 39%; \(p=0.105\)).

**Measure of benefits used in the economic analysis**

The measure of benefit used was the quality-adjusted life-years (QALYs). The authors used a regression equation that also incorporated gender, age and distance visual acuity from eyes in order to assess time trade-off (TTO) utility. Values were assigned by 224 consecutive patients with AMD who were interviewed by trained researchers in a standardised fashion using TTO boards. The utility data were evaluated at baseline and at one year after treatment.

**Direct costs**

The health care costs in the analysis comprised the initial physician visit (including the cost of a physician assessment, fluorescein angiography and photography) and the follow-up physician visits. The latter included the costs of physician injection, anecortave, angiography and photography in the case of anecortave treatment, and the costs of PDT administration, verteporfin, angiography and photography in the case of PDT. The costs associated with the risk of falls and depression, and with the support and rehabilitative devices used by the patients, were also included in the analysis. Fixed costs, such as administration costs and capital expenditures, were not included. The unit costs were reported and were derived from official published sources and from the literature. The quantities of resources used were derived from the ongoing clinical trial. Since the costs were incurred during one year, discounting was not relevant. The price year was not explicitly reported.

**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 threshold analysis to evaluate the incremental cost-effectiveness of the new treatment. Specifically, they aimed to estimate the cost of the new treatment option that would result in ICERs of $100,000, $50,000, $20,000 and $0 per QALY.

**Estimated benefits used in the economic analysis**

Over the 1-year time horizon all treatment options resulted in the same benefits. In particular, patients in all treatment
groups lost 0.02 QALYs during the 1-year period.

**Cost results**
The costs were reported per patient. The total cost for PDT was $12,722 per patient over the 1-year period, while the total cost of the anecortave treatment option was $6,823 plus 2 times the cost of anecortave.

**Synthesis of costs and benefits**
The authors reported only the results of the threshold analysis. This demonstrated that pre-vial costs of anecortave of $3,022, $2,986, $2,964 and $2,950 would result in ICERs of $100,000, $50,000, $20,000 and $0 per QALY, respectively, compared with PDT.

For patients in the group of no reflux who received their retreatment injection within 182 days of the first injection, a pre-vial cost of anecortave of $2,986 would result in an ICER of $50,000 per QALY.

**Authors' conclusions**
There was no statistically significant difference in visual stabilisation between those who received anecortave and those who received photodynamic therapy (PDT). A hypothetical cost of anecortave of $2,986 per vial would be associated with an incremental cost-effectiveness ratio (ICER) of $50,000 per quality-adjusted life-year (QALY), a generally accepted threshold ICER.

**CRD COMMENTARY - Selection of comparators**
The selection of the comparator was explicitly reported. PDT seems to have represented standard practice in the authors' setting. You should decide if this represents a valid health technology in your own setting.

**Validity of estimate of measure of effectiveness**
A systematic review of the literature was not undertaken. In particular, estimates of effectiveness were derived from an ongoing clinical trial and from data presented at a conference meeting. Although it is common practice in modelling studies not to conduct a systematic review, it does not always ensure that the best data available are used in the model. The authors appear to have used the available data selectively, and they did not report much of the methodology used in their review. Differences between different sources of data were not investigated. In addition, the characteristics of the patients were not reported, thus limiting the generalisability of the results to other settings. The authors also did not conduct sensitivity analyses to test the robustness of their results.

**Validity of estimate of measure of benefit**
The measure of benefit used was the QALYs measured over a 1-year period, as derived from the decision tree model. This was appropriate for the study question. The utility values were derived from patient interviews based on TTO boards, and were not explored in sensitivity analyses.

**Validity of estimate of costs**
The authors reported that the study had been conducted from a societal perspective. However, the indirect costs were not included. Only variable incremental costs were included in the model, while fixed costs were omitted as they were assumed to be equal in both treatment arms. The unit costs were reported, but no sensitivity analysis around the costs was conducted to assess the robustness of the estimates used. A statistical analysis of the quantities was also not performed, which may introduce possible uncertainty into the results. Although the costs were derived from various sources and related to different dates, the costs were not appropriately inflated and the price year was not reported, hence impeding any future reflation exercises.
Other issues
The authors did not compare their results with those from other studies. However, this might have been due to a lack of literature in the same area. The issue of generalisability of the results to other settings was not addressed. The authors do not seem to have presented their results selectively. The authors reported two main limitations to their study. First, the utility values were not collected directly from patients in the Phase III clinical trial but were based on secondary data. Second, the model did not take differential economic costs associated with treatment-related adverse effects into consideration.

Implications of the study
The authors did not make any explicit recommendations for changes in policy or practice, or for further research. However, the discussion highlighted areas where more information is needed.

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