Cost-effectiveness analysis of glatiramer acetate in the treatment of relapsing-remitting multiple sclerosis

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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
The use of glatiramer acetate (GA) to treat relapsing-remitting multiple sclerosis (RRMS). RRMS was defined as relapses with either full recovery or some residual deficit upon recovery, and no disease progression in the period between relapses.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis; cost-utility analysis.

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

Setting
The setting was secondary care. The economic study was carried out in the UK.

Dates to which data relate
The effectiveness and resource use data were derived from studies published between 1991 and 2001. The cost data came from studies published between 1998 and 2001. The price year was 2000.

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

Outcomes assessed in the review
The outcomes estimated from the literature were:

- the number of relapses,
- the change in the disability score (Expanded Disability Status Scale, EDSS),
- the natural history mean time to progression for EDSS projection,
- the utility weights for specific EDSS states, and
- utility losses associated with relapses.
Study designs and other criteria for inclusion in the review
It was not stated whether a systematic review of the literature had been undertaken to identify the primary studies. The evidence for GA was derived from a randomised, placebo-controlled, double-blind trial (for up to 35 months, then open label). The data on BSC were derived from a longitudinal follow-up of 1,099 consecutive patients. The utility of life data came from a sample of 102 patients, using both disease-specific (MSQOL-54) and generic (EQ-5D) quality of life questionnaires.

Sources searched to identify primary studies
Not stated.

Criteria used to ensure the validity of primary studies
The validity of the evidence was implicitly ensured by the design of the clinical trial. However, no specific criteria were used to ensure the validity of the primary sources.

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

Number of primary studies included
Six primary studies provided the evidence.

Methods of combining primary studies
The primary studies appear to have been combined using a narrative method.

Investigation of differences between primary studies
The authors stated that data on placebo were derived from a sample of patients compatible with the clinical data for GA.

Results of the review
During the first 35 months of the trial, the adjusted mean number of relapses per patient was 1.34 with GA and 1.98 with placebo (32% reduction). Over 6 years, the annual relapse rate with GA was 0.42 (72% reduction from annualised relapse rates before randomisation). In the follow-up of the study, the annual relapse rate with GA was 0.23. Further, 25.7% of patients remained relapse-free for the entire study period, while 76.2% had three or fewer relapses in 6 years. The data on neurological disability showed that 29.4% of placebo patients experienced a deterioration of EDSS scores for 3 months, while only 23.2% of GA patients did so during the clinical trial.

The mean time to progression was:

8.97 years for EDSS level 1,
3.31 years for EDSS level 2,
2.02 years for EDSS level 3,
1.22 years for EDSS level 4,
1.25 years for EDSS level 5,
3.89 years for EDSS level 6,
6.52 years for EDSS level 7, 
2.64 years for EDSS level 8, and  
2.80 years for EDSS level 9. 

The utility weights were: 
0.85 for EDSS level 1, 
0.76 for EDSS level 2, 
0.71 for EDSS level 3, 
0.66 for EDSS level 4, 
0.52 for EDSS level 5, 
0.49 for EDSS level 6, and 
0.35 for EDSS level 7. 

The average utility loss per relapse was 0.083. 

**Methods used to derive estimates of effectiveness**  
The authors made some assumptions to derived estimates of effectiveness that were not available in the literature.

**Estimates of effectiveness and key assumptions**  
It was estimated that the utility weight for EDSS level 0 was 1. The duration of relapse was assumed to have been 2 months. Patients in the BSC group were assumed to experience the mean relapse rate of the trial for the placebo group, with relapses equally spaced over the projection period.

**Measure of benefits used in the economic analysis**  
The summary benefit measures used were the disability units avoided, the relapses avoided, and the quality-adjusted life-years (QALYs) gained with GA over placebo. All were derived from published data, as reported already. No discounting was applied.

**Direct costs**  
Discounting was relevant because the costs were incurred during a time period longer than 2 years. However, no discounting was carried out in the base-case. The unit costs were presented separately from the quantities of resources used for a few items only. The health services included in the economic evaluation were GA, treatment of relapse and remission, and caregivers. The perspective of the NHS was adopted in the study. The costs were derived from the Monthly Index of Medical Specialties, Personal Social Services Research Unit, and two published studies. The resource use data were derived from published evidence and authors' assumptions. The price year was 2000.

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

**Indirect Costs**  
The indirect costs were not considered in the economic evaluation.
Currency
UK pounds sterling (GB£).

Sensitivity analysis
Univariate sensitivity analyses were carried out to examine the robustness of the estimated cost-effectiveness and cost-utility ratios to variations in the base-case assumptions, such as duration of relapse (which in turn affects utility loss), discounting (both costs and benefits with similar or different rates), and the cost of relapse (doubled in comparison with the base-case estimates).

Estimated benefits used in the economic analysis
The estimated benefits were not reported.

Cost results
The total costs associated with GA and placebo were not reported.

Synthesis of costs and benefits
Incremental cost-effectiveness and cost-utility ratios were calculated to combine the costs and benefits of GA relative to BSC. The incremental cost per disability unit avoided was 11,935 for 6 years and 8,862 for 8 years (trial follow-up period). The incremental cost per relapse avoided was 13,626 for 6 years and 11,000 for 8 years. The incremental cost per QALY was 28,515 for 6 years and 22,586 for 8 years.

The sensitivity analysis showed that the most striking result was observed when the duration of relapse was reduced to one month. In this case, the incremental cost per QALY was 84,537 for 6 years and 64,636 for 8 years. Variations in the costs of relapse and the discount rate applied to both the costs and benefits did not impact substantially on the results of the base-case.

Authors' conclusions
Glatiramer acetate (GA) was a cost-effective strategy in comparison with best supportive care (BSC) in the treatment of patients with relapsing-remitting multiple sclerosis (RRMS) in the UK.

CRD COMMENTARY - Selection of comparators
The selection of the comparator (BSC) was appropriate as it represented the typical comparator in the studies that evaluated GA. It also allowed the active value of GA to be evaluated. You should decide whether this is a valid comparator in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness evidence came from published studies. It was unclear whether a review of the literature had been undertaken and the primary studies appear to have identified selectively. The design of the primary studies was not reported for all sources, which were combined using a narrative method. The validity of the study was ensured for the clinical trial. The authors stated that the data for placebo were compatible with trial data. The authors stated that, whenever possible, the best available data were used. Some assumptions were also made when literature-based data were not available. Only utility values were varied in the sensitivity analysis. Therefore, there remained some uncertainty around the other estimators.

Validity of estimate of measure of benefit
The authors justified the choice of the summary benefit measures. QALYs were used because they are a measure of...
comparable with the benefits of other health care interventions. The steps in the calculation of the QALYs were reported. However, it was noted that, owing to the nature of the disease, the impact of the treatment on relapse and disability levels was more appropriate. Therefore, both were considered relevant benefit measures.

Validity of estimate of costs
The authors stated explicitly the perspective taken in the study. As such, it appears that all the relevant categories of costs have been included in the economic evaluation. However, there was limited on the unit costs and quantities of resources used, and some costs were presented as macro-categories. This reduces the possibility of replicating the analysis. The source of the data was reported for all items. Discounting could have been relevant because of the long time horizon of the analysis. However, a discount rate was applied only in the sensitivity analysis and this did not have a strong impact on the final results. The price year was reported, which aids reflation exercises in other settings. Statistical analyses of the costs were not carried out but variations in the main cost driver (i.e. cost of relapse) were investigated in the sensitivity analysis.

Other issues
The authors did not make extensive comparisons of their findings with those from other settings. It was highlighted that RRMS, by its own nature, is a fluctuant disease and the impact on individual patients could be very different. Therefore, caution is required when generalising the results of the current analysis to all patients suffering from RRMS. Few sensitivity analyses were performed, which reduces the external validity of the analysis. The authors noted that the choice of restricting the time horizon of the analysis to the trial follow-up period represented a strength of the study because it avoided the use of assumptions to make long-term extrapolations.

Implications of the study
The study results suggested that GA could be considered a feasible treatment option for patients with RRMS. It led to improvements in both relapse rates and disability status.

Source of funding
None stated.

Bibliographic details

Other publications of related interest

Indexing Status
Subject indexing assigned by CRD

MeSH
Chronic Disease; Comparative Study; Cost-Benefit Analysis; Costs and Cost Analysis; Economics, Pharmaceutical; Great Britain; Multiple Sclerosis /drug therapy; Prospective Studies; Quality of Life; Recurrence; Sensitivity and Specificity; Treatment Outcome

AccessionNumber