Economic impact of enoxaparin after acute ischemic stroke based on PREVAIL

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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 assessed the economic impact of low-molecular weight heparin (LMWH; enoxaparin), compared with unfractionated heparin, for the prevention of venous thromboembolism after acute ischaemic stroke, using the clinical findings from the Prevention of Venous thromboembolism after Acute Ischaemic stroke with LMWH enoxaparin (PREVAIL Study). Enoxaparin reduced the clinical and economic burden of venous thromboembolism and was cost-effective from the payer perspective. The analysis focused on the costs and these calculations were well carried out, making the authors' conclusions robust.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
The objective was to assess the economic impact of low-molecular weight heparin (LMWH; enoxaparin), compared with unfractionated heparin, for the prevention of venous thromboembolism (VTE) after acute ischaemic stroke, using the clinical findings from the Prevention of VTE after Acute Ischaemic stroke with LMWH Enoxaparin (PREVAIL Study).

Interventions
Enoxaparin (40mg subcutaneously, once daily) was compared against unfractionated heparin (5,000 units subcutaneously, every 12 hours for 10 days).

Location/setting
USA/hospital.

Methods
Analytical approach:
The analysis was based on a decision-tree model. The authors stated that they took the perspective of the health care payer.

Effectiveness data:
The clinical evidence came from the PREVAIL Study, which was an open-label, randomised, controlled trial (RCT) of 1,762 patients who received either enoxaparin or unfractionated heparin after acute ischaemic stroke. The data on the treatment effect in preventing VTE and on the safety of medication (intracranial or extracranial bleeding) were directly from this trial. The primary endpoint was a composite measure of the rates of symptomatic and asymptomatic deep-vein thrombosis (DVT), symptomatic pulmonary embolism, and fatal pulmonary embolism.

Monetary benefit and utility valuations:
Not considered.

Measure of benefit:
The main clinical endpoint was the rate of any clinical event (DVT, fatal or non fatal pulmonary embolism, minor or major haemorrhage, or death).

Cost data:
The economic analysis included the costs of drugs and the treatment of clinical events (VTE, pulmonary embolism,
intracranial haemorrhage, major extracranial haemorrhage, minor haemorrhage, or death). The rates of clinical events were from the PREVAIL Study and the costs were the median values from the Centers for Medicare and Medicaid Services claims information, classified by US diagnosis-related group. The drug costs were the US average wholesale prices in 2008, with dosages from the PREVAIL Study. Three cost calculations were used, based on the definition of VTE: from the PREVAIL Study; major and minor VTE; and from the European Committee for Medicinal Products for Human Use (CHMP). All costs were in US dollars ($).

Analysis of uncertainty:
The analysis of uncertainty focused on changes in the economic inputs, using univariate and multivariate (Monte Carlo simulation) sensitivity analyses. Ranges of ±20% were used. Triangular distributions were applied for the multivariate sensitivity analyses. An analysis was performed classifying patients as having less or more severe stroke, based on a National Institutes of Health Stroke Scale (NIHSS) score of less than 14 (less severe) or 14 or more (more severe).

Results
Enoxaparin reduced the risk of VTE by 43% (to 10.21%) compared with unfractionated heparin (18.09%; RR 0.57, 95% CI 0.44 to 0.76), with an 8% rate of bleeding in each group.

Compared with unfractionated heparin, enoxaparin led to savings of $895 using the PREVAIL Study definition of VTE, $522 using the definition of minor and major VTE, and $517 using the CHMP definition.

Using the PREVAIL definition, the savings were $488 for patients with an NIHSS score of less than 14 and $1,800 for those with a NIHSS score 14 or more.

Changes in model inputs did not alter substantially the base case results. In the multivariate analysis, the cost-savings ranged from under $700 to over $1,110 using the PREVAIL Study definition, from $330 to $712 using the definition of minor versus major VTE, and from under $480 to over $780 using the CHMP definition.

Authors' conclusions
The authors concluded that enoxaparin was cost-effective, from the payer perspective, as it reduced the clinical and economic burden of VTE, compared with unfractionated heparin.

CRD commentary
Interventions:
The rationale for the selection of the comparators was clear as the two available treatments for patients at risk of VTE were selected. The dosages were reported and reflected the treatment patterns in the PREVAIL trial.

Effectiveness/benefits:
The clinical analysis was based on data from the PREVAIL Study and the methods and results of this trial were published elsewhere (Sherman, et al. 2007, see 'Other Publications of Related Interest' below for bibliographic details). In theory, the use of a large head-to-head randomised controlled trial should have ensured high internal validity, but the authors did not state whether other published clinical studies had shown similar or different results. An extensive sensitivity analysis was conducted on the clinical parameters. The analysis had a cost-consequences framework and no summary measure of benefit was used. The key clinical outcomes were appropriate for the disease.

Costs:
The assessment of cost differences between the two treatments was the primary aim of the analysis. The categories of costs were appropriate for the perspective of the health care payer and the sources were valid as they were typical US sources for health care expenditure. The use of Medicare and Medicaid databases provided gross costs only and they were not broken down into individual items. The price year was not reported, which limits the possibility of making reflation exercises for other time periods. Different methods were used to estimate the costs associated with clinical events, and the results were stable to these changes.

Analysis and results:
The results were clearly presented, especially for the economic impact of the two interventions. The clinical and
economic outcomes were not synthesised as a cost-consequences analysis appears to have been conducted, but enoxaparin was dominant as it was less expensive and more effective than unfractionated heparin, which means that the calculation of a cost-effectiveness ratio was not necessary. The uncertainty was satisfactorily investigated, using various appropriate methods, and the findings were clearly presented. The decision model was described and appears to have been appropriate for the short-term analysis. The authors compared their results with those from other published studies that had similar findings. It is likely that these findings will be valid for other settings and their generalisability was not discussed.

Concluding remarks:
The costs were the focus of the analysis and these calculations were well carried out, making the authors’ conclusions robust.

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