Modelling the relative cost-effectiveness of amelogenin in non-healing venous leg ulcers

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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
The objective was to determine whether amelogenin plus compression bandaging was cost-effective compared with compression bandaging alone, for the treatment of venous leg ulcers that had not healed after six months. The authors concluded that amelogenin plus compression bandaging was less costly and more effective than compression bandaging alone, and was, therefore, cost-effective for the National Health Service. Overall, the methodology and reporting were satisfactory and the results appear to be reliable.

Type of economic evaluation
Cost-effectiveness analysis, cost-utility analysis

Study objective
The objective was to determine whether the use of amelogenin plus compression bandaging was a cost-effective strategy compared with compression bandaging alone for the treatment of venous leg ulcers that had not healed after six months.

Interventions
The interventions were amelogenin (0.5ml for ulcers under 10cm² and 1ml for ulcers greater than 10cm²) plus compression bandaging versus compression bandaging alone.

Location/setting
UK/secondary care.

Methods
Analytical approach:
A state transition Markov model was constructed to synthesise the data, some of which was extrapolated from a single randomised controlled trial. A 12-month time horizon was adopted and the authors stated that the perspective was that of the UK National Health Service (NHS).

Effectiveness data:
The clinical data came from a single, randomised controlled trial, which compared 42 patients treated with amelogenin and compression bandaging with 41 controls treated with compression bandaging alone (Vowden, et al. 2006, see 'Other Publications of Related Interest' below for bibliographic details). The trial followed-up patients for 24 weeks after the start of treatment. Ulcer size was measured weekly up to week 12 of treatment and then at 24 weeks. Recurrence rates were estimated using 12 studies identified by a review of the literature. The main clinical parameter was the mean ulcer size in square centimetres.

Monetary benefit and utility valuations:
The utility valuations were obtained from a single published study, which presented utility values from members of the general public based on standard gamble methodology for venous leg ulcers (Clegg, et al. 2007, see 'Other Publications of Related Interest' below for bibliographic details).

Measure of benefit:
The measure of benefit was quality-adjusted life-years (QALYs) gained.

Cost data:
The price per vial for the two doses of amelogenin was reported. The authors stated that the direct health care costs were estimated by allocating 2006 to 2007 prices from nationally published UK unit reference costs to the resource use estimates from the Markov model. The resource use in weeks nine to 12 of the trial were used to forecast the resource use up to week 52.

Analysis of uncertainty:
One-way and two-way sensitivity analyses were performed by varying the model parameters of the probability of healing, utility values for different ulcer states, probability of recurrence, and the number of clinician visits.

Results
The expected health care cost of amelogenin plus compression therapy was £3,816 per patient, and the estimated mean health gain per patient was 0.800 QALYs (95% CI 0.768 to 0.834). The expected health care cost of compression therapy alone was £4,261 per patient and the estimated mean health gain per patient was 0.746 QALYs (95% CI 0.746 to 0.781).

Amelogenin was the dominant treatment, which means it was less costly and more effective.

The authors reported that the parameters which most influenced the results were the probability of healing, the number of nurse visits, and the utility values. For example, varying the probability of healing (base case 0.60) from 0.30 to 0.75 caused the cost per QALY gain to vary from -£44,000 to -£7,200. Amelogenin plus compression remained dominant in all cases.

Authors’ conclusions
The authors concluded that amelogenin plus compression bandaging was expected to be cost-effective for the NHS compared with compression bandaging alone for the management of chronic non-healing venous leg ulcers of greater than six months duration.

CRD commentary
Interventions:
The intervention was well described, but it was not clear how often the dressings were changed and amelogenin applied.  [Comment from author: This varied for each patient according to clinical need but further details can be obtained from the publications of the clinical trial (Vowden et al 2007 and Romanelli et al 2008 - see 'Other Publications of Related Interest’ below for bibliographic details)]. The analysis appeared to compare the intervention with the current practice in the study setting and these two alternatives are likely to be generalisable to other settings.

Effectiveness/benefits:
The effectiveness data primarily came from a single study, and most of the details were provided. It was quite a small study and no details were given on the power calculation and the study's potential to show a significant finding. It was also unclear whether this study was the only available randomised controlled trial or the appropriate data source. A review of the literature was conducted, but it would appear that this was only for the recurrence rates. The method and perspective of the utility valuations were provided, but more details of the health state utility valuations and values from the published source could have been provided.  [Comment from author: The utilities were obtained by the authors and were reported elsewhere (Clegg et al 2007 - see 'Other Publications of Related Interest’ below for bibliographic details)].

Costs:
The authors reported the perspective and calculated the direct costs, which were appropriate for the perspective of the NHS. All the relevant costs appear to have been included, and the base year for the costs was clearly defined. The source of the cost per vial of amelogenin was not referenced.

Analysis and results:
: The analytical approach was satisfactory and the model structure was adequately reported, with a diagram. The results were presented clearly and in full, and appropriate one- and two-way sensitivity analyses were performed and reported. The sensitivity analysis could have been improved by a probabilistic sensitivity analysis to fully capture the impact on the results of parameter uncertainty [Comment from author: this was performed - Figure 6 in the original paper]
The base-case estimates of the cost and effectiveness data were reported. The authors acknowledged a number of limitations to their study and they discussed the possible budget implications of their results.

Concluding remarks:
Overall, the methodology and reporting were satisfactory and the results appear to be reliable.

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