An economic assessment of Apligraf (Graftskin) for the treatment of hard-to-heal venous leg ulcers

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 Apligraf (Graftskin) for the treatment of hard-to-heal venous leg ulcers.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study investigated 18 to 89-year-old patients, with venous insufficiency associated with non-infected partial and/or full thickness skin loss ulcers of longer than 1 month's duration that had not adequately responded to conventional ulcer therapy.

Setting
The setting was hospital. The economic study was carried out in the USA.

Dates to which data relate
Effectiveness data were collected from a trial published in 1998. Resource use data were taken from a survey of 14 physicians. Cost data were based on 1996 data sources. The price year was 1996.

Source of effectiveness data
Effectiveness evidence was obtained from a single study.

Link between effectiveness and cost data
The costing was undertaken on the same patient sample as that used in the effectiveness analysis. The costing was carried out retrospectively after the effectiveness results were known.

Study sample
Two hundred and forty 18- to 89-year-old patients, with venous insufficiency associated with non-infected partial and/or full thickness skin loss ulcers of longer than 1 month's duration that had not adequately responded to conventional ulcer therapy, received either Graftskin or compression therapy using Unna's boot.

Study design
The study was a prospective, multicentre, randomised, controlled trial carried out at a single centre.

**Analysis of effectiveness**
The analysis of the clinical study was based on intention to treat. The primary health outcomes used included the cumulative probabilities of ulcer healing for patients treated with Graftskin and Unna's boot, and the probabilities of adverse events and recurrence. The authors did not state whether, at analysis, groups were comparable in terms of demographic characteristics.

**Effectiveness results**
The cumulative probabilities of ulcer healing for patients treated with Graftskin varied between 0.0972 by the end of the first month and 0.5694 by the end of the first year.

The cumulative probabilities of ulcer healing for patients treated with Unna's boot varied between 0.0625 by the end of the first month and 0.3125 by the end of the first year.

The probability of adverse events was 0.087 with Graftskin and 0.052 with Unna's boot.

The probability of discontinuation of therapy as a result of adverse events was 0.006 with Graftskin and 0.030 with Unna's boot.

The probability of recurrence was 0.030 with Graftskin and 0.037 with Unna's boot.

**Clinical conclusions**
Graftskin is more effective than Unna's boot for treating patients with ulcers that had been present for at least one year.

**Modelling**
A 12-month, semi-Markov decision analytic model was used to determine the cost-effectiveness of the treatment strategies.

**Measure of benefits used in the economic analysis**
The number of months spent in the healed state and the percentage of each group of patients whose ulcers were healed at the end of the year were used as the measures of benefit.

**Direct costs**
Direct costs were not discounted given the short time frame of the study (less than 1 year). Quantities and costs were reported separately. Direct costs included costs of the therapeutic option, additional compression dressings, physician office visits, home health visits, laboratory tests and procedures, management of adverse events, and hospitalisations. The quantity/cost boundary adopted was that of a commercial health plan with first-dollar coverage. The estimation of quantities and costs was based on actual data. Costs were collected from the 1996 Physician Fee and Coding Guide, the 1996 Red Book, the Nationwide Inpatient Sample, and the Medicare National Limits for Clinical Labs. Costs for Graftskin were obtained from Novartis Pharmaceuticals Corporation. The price year was 1996.

**Statistical analysis of costs**
No statistical analysis of costs was reported.

**Indirect Costs**
Indirect costs were not included.
Currency
US dollars ($).

Sensitivity analysis
One-way and multiple sensitivity analyses were conducted on probabilities and costs.

Estimated benefits used in the economic analysis
Treatment with Graftskin led to 4.60 healed months during one year compared with 1.75 healed months for those treated with Unna's boot. Of those patients treated with Graftskin, 48.1% remained healed by the end of one year, compared with 25.2% of those treated with Unna's boot.

Cost results
The annual cost of treatment was $20,041 for those managed with Graftskin and $27,493 for those treated with Unna's boot.

Synthesis of costs and benefits
Graftskin was the dominant strategy. These results were sensitive to changes in the unit cost of hospitalisation for patients receiving Graftskin and resource-use estimates.

Authors' conclusions
Graftskin was both more effective and less costly than Unna's boot for treating patients with ulcers that had been present for at least a year.

CRD COMMENTARY - Selection of comparators
A justification was given for the comparators used namely that they were currently employed strategies. You, as a user of the database, should decide if these health technologies are relevant to your setting.

Validity of estimate of measure of benefit
The analysis was based on a randomised-controlled trial, which was appropriate for the study question. The study sample was representative of the study population. However, the authors did not report whether patient groups were comparable at analysis, which may have influenced the results if this were not the case. Estimation of benefits was appropriately obtained directly from the effectiveness analysis.

Validity of estimate of costs
All relevant direct cost categories were included but it should be noted that direct non-medical, indirect, and intangible costs were not considered. Sensitivity analyses were conducted on costs and quantities; quantities and costs were reported separately; and the price year was reported. However, charges were used to proxy prices, which limits the generalisability of the results.

Other issues
The authors did not make appropriate comparisons of their findings with those from other studies and did not specifically address the issue of the generalisability of their results to other settings. The authors did not present their results selectively. The study considered patients with hard-to-heal venous leg ulcers and this was reflected in the authors' conclusions. The authors suggested that the implications of the trend towards reduced resource use are that the Graftskin strategy may cost less in practice than the model suggests in the base case.
Implications of the study
Within the caveats mentioned above, the findings of this study suggest that Graftskin is the dominant strategy over compression therapy using Unna's boot.

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