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
This study compared four 20-week treatments for diabetic neuropathic foot ulcers:

- standard care (SC) of wounds in a primary care setting;
- standard treatment in a specialised wound care centre (WCC);
- treatment with becaplermin gel 0.01% (a recombinant growth factor preparation);
- treatment with platelet releasate (PR) at a wound care centre.

The study also compared treatment with platelet releasate (PR) at a wound care centre (32 weeks) to standard treatment in a specialised wound care centre (WCC) (32 weeks).

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised diabetics with neuropathic foot ulcers of at least 8 weeks' duration. The 8 week duration inclusion criteria applied to the WCC and PR treatments, but it was not clear whether it also applied to the other two treatments. Wounds with osteomyelitis were excluded from the becaplermin and SC populations.

Setting
The setting was primary care and specialist wound care centres. The economic analysis was carried out in the USA.

Dates to which data relate
The effectiveness evidence for SC and becaplermin were published in 1999 and 1998, respectively. The data for WCC and PR were published in 2000. The prices of health services and durable equipment were from 1999. No date was reported for the medication prices.

Source of effectiveness data
The effectiveness data for SC and becaplermin were collected from a separate meta-analysis. The data for WCC and PR were collected from a validated database of 26,000 patients who attended wound care clinics with diabetic foot ulcers.
Outcomes assessed in the review
The outcomes assessed were the percentage of ulcers healed after 20 and 32 weeks of care.

Study designs and other criteria for inclusion in the review
The SC data were derived from a published meta-analysis of clinical trials. The becaplermin data were obtained from a meta-analysis of published studies of becaplermin gel 0.01% conducted by the authors. It was not stated whether these were clinical trials or observational studies. The WCC and PR data were derived from a clinical database, and only patients with ulcers of at least 8 weeks duration were included in the analysis.

Sources searched to identify primary studies
Not reported.

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
Two meta-analyses were included.

Methods of combining primary studies
The data on each of the four treatments came from a separate source. Therefore, no data were combined.

Investigation of differences between primary studies
The authors did not address the differences between the two meta-analyses. However, they commented on the fact that, while the data from the meta-analyses were from clinical trials, the database data were observational in nature and may be subject to selection bias. Therefore, the effectiveness of PR may be underestimated relative to WCC treatment, and the efficacy of PR and WCC treatment may be underestimated relative to SC or becaplermin.

Results of the review
At 20 weeks, the percentages of ulcers healed were:

- SC, 30.9% (95% CI: 26.6 - 35.1);
- becaplermin, 43% (95% CI: 37.3 - 48.7);
- PR, 36.8% (95% CI: 35.4 - 38.2); and
- WCC, 35.6% (95% CI: 34.8 - 36.4), respectively.

At 32 weeks, the percentages of ulcers healed were:

- PR, 48.4% (95% CI: 46.9 - 49.8); and
- WCC, 38.0% (95% CI: 37.2 - 38.8).
Measure of benefits used in the economic analysis
The measure of benefits was the percentage of ulcers healed.

Direct costs
The cost analysis included the direct health care costs incurred by all payers. Components of each treatment included physician visits, debridement of wounds, shoe inserts, crutches, gauze/tape, becaplermin and PR medications. For each treatment, the cost of each component was reported separately. The costs of health services were derived from the Medicare Resource-Based Relative Value Unit Scale for Pennsylvania for the first quarter of 1999. The costs of durable medical equipment were taken from the 1999 fee schedule for Pennsylvania. The cost of becaplermin was the average wholesale price. The cost of PR was obtained by personal communication with the database managers. Unit costs were not reported separately from quantities.

The estimation of resource use made assumptions about the frequency of follow-up visits and debridement: most patients visit their physician every 2 weeks and are debrided at this time. The derivation of the resource use data for medications and equipment was not stated.

The study reported the average costs per patient. Discounting was not relevant as the time period was less than one year.

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

Indirect Costs
Indirect costs were not included in this analysis.

Currency
US dollars ($).

Sensitivity analysis
One-way sensitivity analyses were carried out to test the robustness of the assumptions about resource use, cost and uncertainty in treatment effectiveness. The parameters varied were the costs of PR and becaplermin (costs were halved and doubled), the number of physician visits and debridements (increased and decreased, but the range was not reported) and the effectiveness estimates for each therapy (using the 95% confidence interval limits).

Estimated benefits used in the economic analysis
The benefits were the percentage of ulcers healed after 20 weeks (all treatments) and 32 weeks (PR and WCC treatment only) of care. Side effects of treatment were not considered.

Cost results
After 20 weeks of care, the total per patient costs were $1,759.28 (SC), $2,201.99 (becaplermin), $4,204.26 (PR) and $1,677.64 (WCC).

At 32 weeks, the costs were $5,192.98 (PR) and $2,241.43 (WCC).

These were treatment costs, not including any adverse effects. All costs are in 1999 US dollars.

Synthesis of costs and benefits
The authors combined costs and benefits as the incremental cost per patient of increasing the chance of healing at 20 or
32 weeks by 1%. The incremental costs per additional 1% of ulcers healed (most expensive versus least expensive) were $36.59 (SC versus becaplermin; 20 weeks), $414.40 (SC versus PR; 20 weeks), $70.86 (becaplermin versus WCC; 20 weeks), $2,105.52 (PR versus WCC; 20 weeks) and $283.80 (PR versus WCC; 32 weeks). At 20 weeks of care, becaplermin dominated PR, being both more effective and less costly.

The absolute cost-effectiveness of the therapies was sensitive to changes in cost, although the relative cost-effectiveness of the therapies was not. The results were sensitive to the effectiveness of PR at 20 weeks.

**Authors’ conclusions**
Treatment with becaplermin or PR is more effective and costly than WCC treatment. Becaplermin, PR and WCC treatment are all more effective than SC. At 20 weeks, becaplermin was more effective and less costly than PR.

**CRD COMMENTARY - Selection of comparators**
No treatment was explicitly chosen as a comparator. It was implied that standard care in a primary care setting (SC) is the more common current practice in the USA. You, as a user of this database should consider how this compares to current practice in your own setting.

**Validity of estimate of measure of effectiveness**
The authors did not state that a systematic review of the literature had been undertaken. The authors used one study or source to obtain data for each treatment. The authors did not consider the impact of differences between the primary studies when estimating effectiveness. The authors noted that the main limitation of this study was that the effectiveness data were taken from different types of sources and compared directly with one another. The effectiveness data for SC and becaplermin were taken from meta-analyses (presumably of clinical trials) reporting efficacy. The data for PR and WCC treatment were obtained from a large database and were observational in nature, relating to effectiveness rather than efficacy, and may have been affected by selection bias. The authors noted that patients in the PR group might have begun this treatment after "several weeks" of WCC. Thus, the data for PR patients at 20 weeks may include patients who have received PR for less than 20 weeks. These factors may underestimate the effectiveness of PR, a parameter to which the cost-effectiveness results were shown to be sensitive.

**Validity of estimate of measure of benefit**
The estimation of benefits was obtained directly from the effectiveness analysis. The 20-week endpoint for healed ulcers represents a standard effectiveness measure, reported in several clinical trials and meta-analyses. The study measure of benefit (percentage of ulcers healed) is specific to diabetic foot ulcers and does not allow the cost-effectiveness of these treatments to be compared with those in other disease areas. The authors noted that there has been no research on what society might be willing to pay for a 1% increase in ulcers healed.

**Validity of estimate of costs**
The cost analysis included direct costs relevant to the perspective of the payer. Costs and quantities were not reported separately. The derivation of resource use data was unclear although sensitivity analysis was carried out on some resource use and cost parameters (results not reported). The unit costs were taken from published sources and reflected costs rather than charges. The price year was reported for all resources except medications.

**Other issues**
The authors mentioned an earlier cost-effectiveness study of PR versus WCC but did not compare their findings with those from this study. The authors stated that their data, including those derived from the large database, may not be generalisable to all patients with diabetic foot ulcers although this point was not fully explained. The authors did not present their results selectively.
Implications of the study
The authors recommend that further research be carried out to obtain better estimates of the effectiveness of PR since the findings of this study were shown to be sensitive to this parameter.

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Other publications of related interest


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