Cost-effectiveness of becaplermin for nonhealing neuropathic diabetic foot 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.

Health technology
The strategy of adding becaplermin to best clinical care for the treatment of non-healing ulcers in patients with adequately controlled diabetes, adequate oxygen supply to the surrounding tissue, and no infection or nonvitalised tissue in the ulcer, was under evaluation.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised adult patients with diabetes mellitus, Type 1 or Type 2, and a foot ulcer. The foot ulcer had to have been present for at least 8 weeks, be full-thickness (to subcutaneous fat), and be free of local wound infection, cellulitis or osteomyelitis. It also had to have been debrided to remove callus, necrotic debris and slough.

Setting
The setting was the community. The economic study was carried out in Ontario, Canada.

Dates to which data relate
The dates to which the effectiveness data related were not reported. The costs were estimated in 1998 and updated to 2002 costs using the Canadian Consumer Price Index for Personal and Health Care.

Source of effectiveness data
The effectiveness data were derived from a single study, completed and published by other authors (Wieman et al., see Other Publications of Related Interest).

Link between effectiveness and cost data
The costing was undertaken retrospectively. The health resource use data were collected separately using a modified Delphi approach.

Study sample
The effectiveness data for the study were taken from a "parent" study by Steed et al. (1995) and Wieman et al. (1998) (see Other Publications of Related Interest). The authors did not report that power calculations were carried out to estimate the impact of chance on the results. It was unclear how the initial sample was selected. There were 251 patients with diabetes participating in the study, 124 in the becaplermin group and 127 in the control group.
Study design
The study was a randomised controlled trial. The trial was double-blind and was carried out in multiple centres. The patients were randomly assigned to each group, but the method of randomisation was not reported. The patients were followed up for a 20-week period. The loss to follow-up was unclear. The reader should consult the parent study for further details that were not reported in the current study.

Analysis of effectiveness
It was unclear whether the analysis was conducted on an intention to treat basis. The primary health outcome was ulcer-days averted. No summary statistics concerning the two patient groups were reported, thus it was unclear whether the groups were comparable at baseline.

Effectiveness results
Patients using becaplermin had a greater chance of 100% ulcer closure by 20 weeks (62 of 124 patients, 50%) than patients receiving vehicle gel alone (44 of 127 patients, 35%), (43% improvement; p=0.007).

For patients whose ulcer did not close, the time to healing was shorter with becaplermin (35th percentile: 86 days versus 127 days; p=0.013). The groups did not differ significantly in adverse events or ulcer recurrence.

Patients who responded to treatment (30% ulcer closure) after 2 months of treatment showed a much higher probability of healing by 20 weeks (62% of responders healed versus 1% of nonresponders).

Clinical conclusions
Becaplermin was more effective than vehicle-only control in healing chronic foot ulcers of patients with adequate vasculature who were receiving best clinical care.

Modelling
A decision tree model was used to structure the estimation of the average number of ulcer-days per patient averted by the addition of becaplermin gel use to best clinical care. The model was divided into two major time periods, 0 to 20 weeks and 21 to 52 weeks.

Measure of benefits used in the economic analysis
The measures of health benefits used were the ulcer-days averted, wound healing and infection risk. These are the same estimates as used in the effectiveness analysis.

Direct costs
The direct costs included the costs for treatments and a fixed cost per patient for special devices and weight offloading equipment. A Delphi panel of health professionals who are actively involved with continuing education in this area, and representing the range of disciplines providing such care, estimated the health resource use associated with the treatment of an ulcer or infection. The unit prices were obtained from standard sources, such as the Ontario Schedule of Benefits for physician services and fully allocated costs of the Hamilton Health Sciences Corporation for hospital services. Prescription drugs were priced according to the Ontario Drug Benefit formulary with appropriate mark-ups and dispensing fees. The costs were estimated in 1998 and updated to 2002 costs using the Canadian Consumer Price Index for Personal and Health Care. Discounting was not carried out as the costs were incurred during one year.

Statistical analysis of costs
The costs were treated deterministically.
Indirect Costs
The indirect costs included the patients' out-of-pocket travel expenses and the cost of time lost from work. In the sensitivity analysis, the cost of time associated with not being able to perform usual unpaid activities was also included as a relevant cost to society. Discounting was not carried out, which was appropriate as the costs were incurred during one year.

Currency
The currency used was Canadian dollars (Can$). The mean exchange rate for 1998 was Can$1.00 = US$0.67.

Sensitivity analysis
One-way sensitivity analyses were carried out to assess the impact of uncertainty and variability in the parameter estimates. The authors considered:

- the proportion of patients healed within 20 weeks,
- the proportion of patients healed between 20 weeks and 1 year,
- the proportion of those unhealed at 20 weeks to heal by 1 year,
- the cost of home care visits, and
- the cost of time associated with not being able to perform usual unpaid activities.

Estimated benefits used in the economic analysis
Over one year, on average, the adding of up to 20 weeks of becaplermin to best clinical care resulted in 26 fewer ulcer-days per patient compared with best clinical care alone. There was also a small reduction in the proportion of infected wounds in patients treated with becaplermin.

The average time to heal over a year was 162 days with best clinical care versus 138 days with best clinical care plus becaplermin.

Ulcer recurrence of those healed was 24% with best clinical care versus 30% with best clinical care plus becaplermin.

The average time for an ulcer to recur was 43 days with best clinical care versus 79 days with best clinical care plus becaplermin.

Cost results
The average annual cost per patient was Can$16,680 in the becaplermin group versus Can$16,513 in the best clinical care group.

The incremental annual cost when using becaplermin was Can$167 per patient.

Synthesis of costs and benefits
The costs and benefits were combined by calculating an incremental cost-effectiveness ratio (i.e. the additional cost required per ulcer-day averted). The study found that incorporating becaplermin with best clinical care resulted in an incremental cost-effectiveness ratio of Can$6 per ulcer-day averted. The results were sensitive to becaplermin cost, efficacy, effect on infection and recurrence rates, and the cost of home care visits. They were also sensitive to the inclusion of a societal cost value for all time lost from usual activities.

Authors' conclusions
Over one year, the addition of up to 20 weeks of becaplermin to best clinical care resulted in a clinical benefit of 26 fewer ulcer-days per patient, along with an increase in the total treatment cost. From the societal perspective, the incremental cost-effectiveness ratio was Can$6 per ulcer-day averted.

**CRD COMMENTARY - Selection of comparators**
The comparator used was justified on the grounds that it represented the best clinical care practice in the authors’ setting. You should decide if this is current practice in your own setting.

**Validity of estimate of measure of effectiveness**
The basis of the analysis was a randomised controlled trial. This was appropriate for the study question, as well-conducted randomised controlled trials are the ‘gold’ standard study design when comparing different health technologies. However, there was limited information on the method of randomisation and there was a lack of summary statistics concerning the patients. It is not possible to assess whether there were systematic differences that might have caused differences in the results between patient groups.

**Validity of estimate of measure of benefit**
The ulcer-days averted were used as the summary measure of health benefit. This was taken directly from the effectiveness analysis.

**Validity of estimate of costs**
All the categories of cost relevant to the perspectives adopted appear to have been included in the analysis. The costs and resource use were reported separately. Resource use was estimated by an expert panel using a modified Delphi approach, which was reported in the study. The unit costs were derived from a variety of different sources. Uncertainty in the costs was then tested by increasing and decreasing them by 50%. Discounting was unnecessary since all the costs were incurred during one year.

**Other issues**
The authors made broad comparisons of their findings with those from other studies that found the healing rates with becaplermin were as high as 60%. They also addressed the issue of generalisability to other settings. The authors do not appear to have presented their results selectively and their conclusions reflected the scope of the analysis. The authors reported an important limitation to their study. More specifically, a model with clinical results from a 20-week trial was extended to a full year and combined with associated cost data based on a Delphi technique.

**Implications of the study**
The authors suggested further investigations into the clinical benefits of becaplermin, to enhance cost-effectiveness information for informed treatment decisions. Decision-makers in other health care systems should investigate the cost-effectiveness of becaplermin in their own setting.

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Other publications of related interest


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