Cost-effectiveness of ziconotide in intrathecal pain management for severe chronic pain patients in the UK
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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 aimed to explore the cost-effectiveness of ziconotide, compared with best supportive care, for the treatment of adult patients with chronic intractable pain. The authors concluded that ziconotide was a cost-effective option. The study had some limitations, but the reporting of the methods and results was satisfactory and an extensive sensitivity analysis was performed to explore the uncertainty in the results. The authors' conclusions reflect the scope of their analysis.

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

Study objective
The objective was to explore the cost-effectiveness of ziconotide, compared with best supportive care, for adult patients with chronic intractable pain.

Interventions
Ziconotide, a non-opioid analgesic, at a dose of 0.26 micrograms per hour (SD 0.19) was compared with best supportive care, which was defined as systemic opioids in combination with other analgesics administered into the spinal fluid. All patients were assumed to have an implanted intrathecal pump; to have tried other single and combination intrathecal analgesics and other less invasive treatment options; and to still have refractory pain.

Location-setting
UK/primary care.

Methods
Analytical approach:
A patient-level micro-simulation model was constructed to assess the clinical and economic impact of the treatment strategies, using evidence from published literature. The model had two phases, which were the three weeks of up-titration and the following period up to a lifetime horizon. The authors stated that the perspective was that of the UK NHS.

Effectiveness data:
The clinical data were from a double-blind randomised placebo-controlled trial of ziconotide for patients aged 27 to 86 years with severe chronic pain that was inadequately controlled by systemic analgesics, intrathecal analgesics, or both. The duration of the trial was three weeks and 112 patients were randomised to ziconotide and 108 to placebo. The placebo arm of the trial supplied the data for best supportive care. The long-term outcomes, including discontinuation and treatment response, were from a trial extension study, two randomised controlled trials, and two open-label extensions of these trials, with up to three years duration, or they were based on expert opinion. The key clinical parameters were the reduction in pain, measured on the visual analogue scale of pain intensity (VASPI), the adverse event rates, and survival. Treatment responders were defined as patients with a 30% or greater decrease in their VASPI score after the three-week up-titration phase. The average age at model entry was 54 years.

Monetary benefit and utility valuations:
The utility estimates were from a tailored study of 103 members of the general population, which used the time trade-
off method to value the health states of chronic pain.

Measure of benefit:
The benefit measure was the number of quality-adjusted life-years (QALYs), which were discounted at an annual rate of 3.5%.

Cost data:
The analysis included the direct medical and social care costs of the treatment of chronic pain, including contacts with health care professionals, drugs, management of adverse events, and routine management. Estimates of mean resource use were derived from a modified Delphi panel of five clinical experts experienced in intrathecal analgesia. The costs were from national resources, such as the British National Formulary, a Unit Costs of Health and Social Care report, and NHS Reference Costs. The price year was 2006 and all costs were reported in UK pounds sterling (£). A rate of 3.5% per annum was used to discount future costs.

Analysis of uncertainty:
The uncertainty was assessed by one-way sensitivity analysis and a probabilistic sensitivity analysis. The results were presented as incremental cost and effect pairs on the incremental cost-effectiveness plane, and as a cost-effectiveness acceptability curve.

Results
The average lifetime cost of treatment with ziconotide was £112,598 compared with £94,734 for best supportive care. The average lifetime QALYs for a patient treated with ziconotide were 1.674 compared with 1.012 for best supportive care.

The incremental cost-effectiveness ratio for treatment with ziconotide was £27,443 (95% CI 18,304 to 38,504) per QALY gained, compared with best supportive care.

At a willingness to pay £20,000 for a QALY, the likelihood that ziconotide was cost-effective was 8.5%, while at £30,000 per QALY, it was 74%. The results were most sensitive to the ziconotide dose per hour and the discount rates.

Authors' conclusions
The authors concluded that ziconotide was a cost-effective treatment for patients with severe chronic pain.

CRD commentary
Interventions:
The interventions appear to have been appropriate; best supportive care was based on placebo treatment, which might have overestimated or underestimated the treatment effect. It was not clear if either option was the usual treatment for these patients. The authors stated that studies using intrathecal morphine did not have comparable populations and an indirect comparison was not feasible.

Effectiveness/benefits:
The methods used to identify and select the clinical studies were not reported. The authors stated that discontinuation assumptions were based on an extensive review of the treatment guidelines at the time and consultation with clinical experts, but the full details were not reported. The effectiveness data were from a range of sources, which were mainly studies with good designs, such as randomised controlled trials, but the study details were only briefly mentioned. A number of sources were of lower quality, such as expert opinion, and assumptions were made for the long-term outcomes. The source for the utility data appears to have been appropriate and the methods used to calculate the QALYs were well described. QALYs were an appropriate benefit measure.

Costs:
The perspective was clearly defined and it appears that all the relevant costs were considered. The sources of unit cost data appear to have been appropriate. The resource use data and costs were presented as category totals, which might restrict the ability to replicate the results in other settings. The costs were appropriately discounted and the cost year was provided.
Analysis and results:
The authors correctly and appropriately used an incremental analysis to determine the cost-effectiveness of the strategies. The parameter uncertainty was assessed in extensive univariate and probabilistic sensitivity analyses. The results were well reported and the authors discussed the main limitations of their analysis, such as that the resource use estimates were based on expert opinion.

Concluding remarks:
Despite the limitations outlined, the analysis was well reported and the methods were appropriate. The uncertainty was satisfactorily assessed in extensive sensitivity analyses on the key model inputs. The authors’ conclusions reflect the scope of the analysis undertaken.

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