Cost-effectiveness of tapentadol prolonged release compared with oxycodone controlled release in the UK in patients with severe non-malignant chronic pain who failed 1st line treatment with morphine


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 evaluated the cost-effectiveness of tapentadol prolonged release, compared with oxycodone controlled release, for severe non-malignant chronic pain in patients for whom controlled-release morphine was ineffective or not tolerated. The authors concluded that tapentadol was less costly and more effective than oxycodone. The study was generally well reported and used appropriate methods. There were some issues stemming from a lack of available evidence, but the authors' conclusion seems plausible for the evidence presented.

Type of economic evaluation
Cost-utility analysis

Study objective
This study evaluated the cost-effectiveness of tapentadol prolonged release, compared with oxycodone controlled release, for severe non-malignant chronic pain in patients for whom controlled-release morphine was ineffective or not tolerated.

Interventions
As a second treatment (after morphine), tapentadol was compared with oxycodone. If this treatment failed, third and fourth treatments could be oxycodone, transdermal fentanyl, transdermal buprenorphine or a combination of oxycodone and naloxone.

Location/setting
UK/out-patient care.

Methods
Analytical approach:
A Markov model was constructed to assess the costs and benefits of tapentadol or oxycodone as the second treatment for chronic pain, over one year, using a 28-day cycle. Severe adverse events or lack of efficacy led to third and fourth treatments. The authors stated that the perspective was that of the UK NHS.

Effectiveness data:
The main effectiveness data were the transition probabilities: withdrawal due to adverse events or lack of efficacy, adverse events without withdrawal, and no withdrawal and no adverse events. With effective treatment, the reduction in pain was assumed to be the same for each drug. For tapentadol and oxycodone, the probabilities were from a pooled analysis of data from three randomised controlled trials of almost 3,000 patients, most of whom (87%) had severe pain at the start. The trials lasted 112 days, so the average probabilities in the fourth cycle were extrapolated to the remaining cycles. The probabilities for third and fourth treatments were from open-label studies identified by a systematic review; the probabilities were only available for the whole study period, so it was assumed that they remained constant.

Monetary benefit and utility valuations:
Utilities were applied to each health state based on adverse events and withdrawal status. EQ-5D utilities were obtained from the three trials of tapentadol and oxycodone. It was assumed that the utility values did not depend on the opioid administered, due to insignificant differences between tapentadol and oxycodone in these trials. The weighted average
for the utility for each state was calculated at the end of the trials.

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

Cost data:
The costs included opioid therapy, physician visits, co-medication and treatment for adverse events. The costs of physician visits, adverse events and co-medication were from a UK medical database and a cohort study. As the severity of adverse events could not be distinguished, the average cost for all adverse events was used. Administration and co-medication costs were assumed to be the same for all opioids. Due to lack of data on fourth-line treatments, these costs were assumed to be the same as the average costs of third-line therapy. Drug costs were from the British National Formulary and the Monthly Index of Medical Specialities. The costs were reported in 2009 to 2010 UK £ and were appropriately inflated.

Analysis of uncertainty:
Probabilistic sensitivity analysis was conducted to evaluate the impact of uncertainty in all of the model parameters on the results. The results were presented on a cost-effectiveness plane and as a cost-effectiveness acceptability curve of the likelihood that the intervention was cost-effective at different willingness-to-pay thresholds. Deterministic sensitivity analyses were conducted to evaluate the impact on the results of varying individual model parameters. The costs were varied by ±50%, and utilities and probabilities were varied by ±20%. Different methods of extrapolating the probabilities beyond the end of the trial were evaluated. The subgroup of patients who had severe pain at the start, was analysed.

Results
The mean cost per patient was £3,542.83 for tapentadol and £3,656.23 for oxycodone. The QALYs per patient were 0.6371 with tapentadol and 0.6237 with oxycodone.

Tapentadol dominated oxycodone, as it was more effective and less costly.

Tapentadol was dominant in the subgroup of patients with severe pain at the start. There was a 85% likelihood that it was dominant for the total population, and a 77% likelihood for the subgroup. It remained dominant in all of the one-way sensitivity analyses, and in the scenarios testing different extrapolation methods.

Authors' conclusions
The authors concluded that tapentadol was less costly and more effective than oxycodone.

CRD commentary
Interventions:
The treatment sequences were clearly described. The comparator (oxycodone) was the active comparator in the trials and the most common opioid in practice, so it was a useful comparison for local decision makers. It was not clear if any relevant alternatives were excluded from the analysis.

Effectiveness/benefits:
The effectiveness and utility values used in the model were clearly reported. The three source trials for the effectiveness of the second-line treatments appear to have been of good quality, but few details were reported. They were referred to as if they were the only relevant trials for tapentadol, but this was not explicitly stated. Due to a lack of available evidence, the data for later treatments were from open-label single-arm trials, which were open to bias. A simple extrapolation was made for the probabilities of withdrawal beyond the ends of these trials, but appropriate sensitivity analyses were conducted to test the impact of this assumption. The specific methods used to derive the utilities were not stated. The authors acknowledged that the utility for an opioid as a later treatment might be lower than as an earlier treatment, but there were no data for the later utility estimates.

Costs:
In general, the costs were clearly reported, with tables of disaggregated costs. No health care resource use was specified, which reduces the transparency and reproducibility of the analysis. Appropriate sources, specific to the UK, were used.
to derive the costs. Future costs and benefits were not discounted, but this was reasonable given the short time horizon. The cost adjustments were adequately reported.

Analysis and results:
The model and results were clearly reported, and uncertainty in the results was appropriately evaluated in the sensitivity analyses. A short time horizon was used; chronic pain is expected to be a long-term condition and the treatments could have an impact on long-term patient outcomes and costs, so the results are unlikely to accurately reflect the long-term cost-effectiveness of the treatments.

Concluding remarks:
The study was generally well reported and used appropriate methods. There were some issues stemming from a lack of available evidence, but the authors' conclusion seems plausible for the evidence presented.

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