Cost effectiveness of paliperidone palmitate versus risperidone long-acting injectable and olanzapine pamoate for the treatment of patients with schizophrenia in Sweden

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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 evaluated the cost-effectiveness of paliperidone palmitate for patients with schizophrenia, who had experienced two or more relapses. The authors concluded that paliperidone was more effective and less costly than both comparators, for a Swedish payer, but data on adherence in practice were needed to validate these results. The study was well reported. Despite the strong results in favour of paliperidone, some uncertainty in its cost-effectiveness remains due to the assumptions and the scope of the interventions.

Type of economic evaluation
Cost-utility analysis

Study objective
This study aimed to evaluate the cost-effectiveness of paliperidone palmitate for patients with schizophrenia, who had experienced two or more relapses (multi-episodes).

Interventions
Paliperidone palmitate long-acting injectable was compared with risperidone long-acting injectable and olanzapine pamoate long-acting injectable. Paliperidone was administered once a month, at a 75mg dose equivalent. Olanzapine was administered every two weeks at a 150mg dose, or every four weeks at a 300mg dose. Risperidone was administered every two weeks at a 37.5mg dose.

Location/setting
Sweden/secondary care.

Methods
Analytical approach:
A Markov model was developed to simulate the ongoing probabilities of not adhering, partly adhering, or fully adhering to treatment, and of relapse and hospital admission, for a cohort of multi-episode patients. The focus of the evaluation was the first treatment choice; up to four sequential choices of therapy were modelled. The time horizon was five years. The authors stated that the perspective was that of the direct medical payer, which was the Swedish health care system.

Effectiveness data:
The main treatment effectiveness data were the risk ratio of relapse, the level of adherence, side-effects (extrapyramidal symptoms, tardive dyskinesia, weight gain and diabetes), and treatment discontinuation. The risk ratio of relapse was from a published mixed-treatment comparison for some therapies, and from several published studies for the other therapies. Adherence rates by treatment and side-effect rates were from observational data. Treatment switch rates were derived from a large observational study.

Monetary benefit and utility valuations:
The utility values for the model health states were from a UK study that used the time trade-off technique on 49 patients with stable schizophrenia and 75 lay people.

Measure of benefit:
The measure of benefit was quality-adjusted life-years (QALYs) gained. Benefits were discounted at an annual rate of
Cost data:
The resource use associated with a relapse was from a six-month comparative UK study. The additional resource use for side-effects was from National Institute for Health and Care Excellence (NICE) guidelines. In-patient resource use was Swedish National data. Drug costs were from the Swedish Pharmaceutical Benefits Agency (TLV). All other unit costs were from regional Swedish sources. All costs were reported in Swedish kronor (SEK). The price year was 2009. The costs were discounted at an annual rate of 3%.

Analysis of uncertainty:
Several one-way sensitivity analyses were conducted, by varying the key parameters by ±25%. Probabilistic sensitivity analysis was conducted by varying every model parameter simultaneously to assess the overall uncertainty in the cost-effectiveness estimate. Cost-effectiveness planes were used to present the results.

Results
Paliperidone resulted in 0.083 more QALYs per person than risperidone; and 0.161 more QALYs per person than olanzapine. Paliperidone cost SEK 19,631 less than risperidone; and SEK 52,726 less than olanzapine.

Paliperidone dominated both comparators, as it was more effective and less costly.

The results were robust to the changes in the parameter values in the sensitivity analyses. Applying a cost-effectiveness threshold of SEK 300,000 per QALY gained, the likelihood that paliperidone was the most cost-effective was 79%.

Authors' conclusions
The authors concluded that paliperidone was estimated to be more effective and less costly than risperidone and olanzapine, from a Swedish payer's perspective. Additional data on adherence rates in practice were needed to validate these results.

CRD commentary
Interventions:
Long-acting injections were assessed as the initial therapy for the population. No short-acting oral therapies were included as initial therapy, so the cost-effectiveness of long-acting versus short-acting therapies was not investigated.

Effectiveness/benefits:
The authors identified studies to supplement a published mixed-treatment comparison, but no information was given on their search terms, sources searched and inclusion criteria, so it was not clear that the best available evidence was used. The effect of risperidone relative to the other treatments was established by assuming equivalence between placebo and haloperidol, based on one study. Paliperidone was assumed to be equivalent to risperidone based on another study. These assumptions increase the uncertainty in the estimates obtained. Rather than assuming equivalence the authors could have taken the effect estimates and incorporated the uncertainty in them. The effectiveness data and their sources were clearly reported. The authors stated that they included relevant health outcomes and costs related to treatment side-effects, which was good.

Costs:
The cost data and their sources were well reported. A lot of the health care use was from UK sources due to lack of Swedish sources, so some of these data may not have been applicable to the Swedish setting. The unit costs were all from local sources appropriate to the study setting. The detailed reporting will allow a comparison of resource use, which improves the generalisability of the study.

Analysis and results:
The model and analysis were well reported. Probabilistic sensitivity analysis was appropriately conducted. Uncertainty surrounding some of the effectiveness estimates was not assessed as they were assumed to be equivalent. It was not clear that the relevant ranges for each parameter were tested in the sensitivity analyses. The authors compared their results with those of other relevant studies. As with most modelling studies, there remained some uncertainty in some of the assumptions and the data. This may not have been fully captured in the analysis, but good reporting made these
limitations explicit.

Concluding remarks:
The study was mostly well reported. Despite the strong results in favour of paliperidone, some uncertainty in the cost-effectiveness of paliperidone remains due to the assumptions and the scope of the interventions.

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