A pharmacoeconomic analysis of sertindole in the treatment of 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
The study compared the cost-effectiveness of sertindole with atypical antipsychotics (aripiprazole, olanzapine, risperidone and haloperidol) in adults with schizophrenia. The authors concluded that sertindole was a well-tolerated, effective and cost-effective treatment in Sweden. Given the information presented, uncertainty surrounding the assumptions and clinical estimates mean that it is difficult to have confidence in the authors' conclusions.

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

Study objective
The aim was to examine the costs and health benefits of sertindole for the treatment of adults with schizophrenia, who were intolerant to their initial antipsychotics and were switching treatment.

Interventions
Sertindole was compared with the atypical antipsychotics aripiprazole, olanzapine, risperidone and haloperidol. The average maintenance doses were sertindole 16mg/day, olanzapine 10mg/day, risperidone 5mg/day, aripiprazole 15mg/day and haloperidol 8mg/day.

Location/setting
Sweden/community care.

Methods
Analytical approach:
A health-state transition Markov model was used to model the ongoing risks of relapse, compliance and adverse events over a five-year time horizon. Clinical evidence was synthesised from several sources. The authors’ stated the study perspective was from a third-party payer, the National Health Insurance Board of Sweden.

Effectiveness data:
No head-to-head trials were available, so indirect comparison techniques were undertaken using data taken from four randomised controlled trials (RCTs; Azorin, et al. 2006, Zimbroff, et al. 1997, Hale, et al. 2000, and Abbot Laboratories, 1995, see ‘Other Publications of Related Interest’ below for bibliographic details). Results of the RCTs of sertindole compared with placebo or a reference drug were used as data inputs to the model. The key clinical outcome was ‘time without relapse’. As efficacy was understood to be similar across the comparator agents, the analysis focused on tolerance outcomes for compliance rates and adverse events such as extrapyramidal symptoms, weight gain and sedation.

Monetary benefit and utility valuations:
Utility estimates for relapse and non-relapse states came from the EQ-5D visual analogue scale administered to participants of the European Schizophrenia Study (Bebbington, et al. 2005, see ‘Other Publications of Related Interest’ below for bibliographic details).

Measure of benefit:
The measures of benefit used were ‘years without relapse’ and quality-adjusted life-years (QALYs) discounted annually at 5%.
Cost data:
Direct medical costs included pharmaceuticals, drug administration and monitoring, primary and community care contacts, outpatient hospital costs, laboratory tests, clinical examinations, treatment of adverse events, and other service costs. Resource quantities were extracted from patient-level data of patients with schizophrenia at the University Hospital of Uppsala, Sweden or estimated by two clinical experts. The unit costs included the pharmacist purchase prices (per daily doses) and various official tariffs. Prices were presented in 2004 Swedish kronor (SEK).

Analysis of uncertainty:
The model parameters were examined with one-way and probabilistic sensitivity analyses. One-way analyses were performed using most data parameters. The probabilistic sensitivity analysis ran 10,000 simulations using beta and normal distributions for model inputs. Scenario analyses were tested with increased compliance rates (10% and 20%), increased costs for adverse events, and by building in relapse rates for non-compliant patients. Sensitivity analysis results were illustrated using cost-effectiveness acceptability curves.

Results
Over five years, for adults with schizophrenia who had relapsed on first antipsychotic treatment, the total costs for sertindole were SEK 1,032,480 compared with SEK 1,046,589 for risperidone, SEK 1,055,295 for haloperidol, SEK 1,055,999 for olanzapine, and SEK 1,060,345 for aripiprazole. The corresponding QALYs were 2.128 for both sertindole and risperidone compared with 2.110 for haloperidol, 2.127 for olanzapine and 2.126 for aripiprazole. The incremental cost-effectiveness analysis for sertindole versus the comparator drugs showed that sertindole was slightly more effective and less costly.

The results of the one-way scenario and sensitivity analyses showed the base findings were insensitive to changes in all parameters. The authors stated there was an 86% probability that sertindole was cost-effective at a willingness to pay of SEK 344,000 (or £30,000 per QALY gained).

Authors’ conclusions
The authors concluded that sertindole was a clinically effective agent for patients with schizophrenia and represented cost-effective care compared with the available pharmacotherapy options in Sweden. Reductions in direct and indirect costs associated with the more favourable tolerability profile of sertindole were the main drivers of the cost-effective results.

CRD commentary
Interventions:
The therapeutic agents compared were well-described and belonged to the same therapeutic drug class. The results may not be generalisable other settings depending on sertindole availability and the relative prices of the comparator drugs.

Effectiveness/benefits:
It was stated that drug-specific inputs of the agents were based on indirect comparisons. This may have just been adverse events, as a model assumption was that no substantial evidence existed to support differential efficacy between atypical antipsychotics. The evidence was not presented; this was not a reason to exclude parameter estimates if they existed. There was no discussion of the comparability of the populations of the different trials in the indirect analysis. There was no discussion of any meta-analytical methods that might have been adopted. The utility values were measured directly on the intended patient group; their results support the authors' statement on similar clinical effects.

Costs:
The resource quantities and unit costs were clearly presented. The measurement of these resources appeared comprehensive and reasonable. The cost perspective appeared broader than third-party as the study included indirect productivity losses and community-based health care. Unit costs were based on publicly available sources.

Analysis and results:
The authors compared their findings with other pharmacoeconomic studies that found similar and contrasting conclusions of sertindole being less expensive than haloperidol. Although the specific values used in the one-way sensitivity analyses were not reported, the scenario analyses gave enough detail to assess the extent of variation in changes to key variables. The authors acknowledged some limitations including: the omission of quality of life.
decrements to adverse events; the omission of dose reductions or elevations from the model; the simplification of real life scenarios (compliance yes/no instead of using a continuum); and use of indirect comparisons due to lack of direct evidence.

Concluding remarks:
The uncertainty surrounding the clinical estimates and assumptions, given the information presented, mean that it is difficult to have confidence in the authors' conclusions.

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