One-year clinical and economic consequences of oral atypical antipsychotics in the treatment of schizophrenia  
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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 objective was to examine the clinical and economic impact of the oral atypical antipsychotics, aripiprazole, olanzapine, paliperidone extended release, quetiapine, risperidone, and ziprasidone, for the treatment of schizophrenia. The authors concluded that paliperidone extended release had the most favourable clinical and economic outcomes. The study was satisfactorily presented and despite some methodological limitations, the authors’ conclusions appear to be valid.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
The objective was to examine the clinical and economic impact of various oral atypical antipsychotics for the treatment of schizophrenia in patients who had suffered an acute exacerbation.

Interventions
The treatments were aripiprazole, olanzapine, paliperidone extended release, quetiapine, risperidone, and ziprasidone.

Location/setting
USA/secondary care.

Methods
Analytical approach:
The analysis was based on a decision model that estimated the costs and benefits of the antipsychotics over a one-year time horizon. The authors stated that the analysis was carried out from the perspective of the health care system.

Effectiveness data:
The key clinical input was the response rate associated with each therapy. These were derived from double-blind, placebo, randomised controlled trials (RCTs), which were identified through a literature review within commonly used electronic databases. No head-to-head trials that included all the medications were found and a common comparator was required. The key details of these trials were reported and they differed in their designs, patients, and length of follow-up. When more than one appropriate RCT was available for a drug, the clinical data were pooled using a weighted average. Other data on discontinuation and adverse events were from a phase I trial. To simplify the model, it was assumed that patients could switch between medications only once per year.

Monetary benefit and utility valuations:
Not included.

Measure of benefit:
The summary benefit measure was the number of additional days with no relapse (stable days).

Cost data:
The economic analysis included the drugs, in-patient services (hospitalisations, day-patient visits, and emergency room visits), and out-patient services (physician visits, mental health clinic visits, social or group therapy visits, nutritionist
visits, and other medications). The costs associated with the management of relevant adverse events were also included. The unit costs were from average wholesale prices. The quantities of resources were based on common drug-use data reported in an official database, supplemented with data from a panel of clinical experts. All costs were in US dollars ($) and the price year was 2008.

Analysis of uncertainty:
Alternative assumptions were considered in a deterministic one-way sensitivity analysis. Alternative drug costs were based on Medicare rates and other assumptions were based on published evidence or authors’ opinions.

Results
The number of stable days per patient was 346.0 with aripiprazole, 348.7 with olanzapine, 349.1 with paliperidone, 347.1 with quetiapine, 347.7 with risperidone, and 345.4 with ziprasidone. The number of relapses per patient was 2.3 with aripiprazole, 2.0 with olanzapine, 2.0 with paliperidone, 2.2 with quetiapine, 2.0 with risperidone, and 2.4 with ziprasidone. The mean number of days of relapse per patient was 19.0 with aripiprazole, 16.3 with olanzapine, 15.9 with paliperidone, 17.9 with quetiapine, 17.3 with risperidone, and 19.6 with ziprasidone.

The total costs per patient were $19,108 with aripiprazole, $18,163 with olanzapine, $16,904 with paliperidone, $18,095 with quetiapine, $17,697 with risperidone, and $19,063 with ziprasidone.

Cost-effectiveness ratios were not calculated as paliperidone extended release was dominant, which means it was more effective and less expensive than the comparators.

The sensitivity analysis showed that paliperidone remained the cheapest and most effective treatment in all scenarios except two. When the response rate of all comparators was changed to the risperidone response rate and olanzapine had fewer days of relapse than paliperidone, the incremental cost per extra day with no relapse for olanzapine over paliperidone was $1,529. When the price of risperidone was decreased to 50% of the brand price, the incremental cost per extra day with no relapse for risperidone over paliperidone was $4.

Authors’ conclusions
The authors concluded that paliperidone extended release had the most favourable clinical and economic outcomes compared with the other oral atypical antipsychotics.

CRD commentary
Interventions:
The selection of the comparators was appropriate as they were the available oral atypical antipsychotics in the USA.

Effectiveness/benefits:
The analysis was based on sources identified through a literature review, the key details of which were reported. RCTs were selected on the basis of characteristics, such as the duration of follow-up and type of clinical outcome. The authors noted that one limitation was the lack of published head-to-head clinical trials, which meant that indirect comparisons were required. This approach is generally limited due to heterogeneity between trials. The use of RCTs was appropriate as they are well designed. Key information on the data sources was given. The benefit measure was disease-specific and might not allow comparisons with the benefits of other health care interventions.

Costs:
The economic analysis was satisfactorily presented and carried out. The cost categories were consistent with the perspective. The unit costs, data sources, price year, and use of alternative estimates from other payers were reported. The cost estimates were treated deterministically and only a few values were varied in the sensitivity analysis.

Analysis and results:
The outcomes were clearly presented and were synthesised, when required, in an appropriate incremental analysis. The investigation of uncertainty was restricted to a univariate approach, which identified the most influential model inputs, but did not allow a comprehensive evaluation of the overall uncertainty. It was stated that the analysis was limited by the lack of a direct comparison between medications in the clinical literature and future studies were required to overcome...
this issue.

Concluding remarks:
The study was satisfactorily presented and, despite some methodological limitations, the authors’ conclusions appear to be valid.

Funding
Supported by Ortho-McNeil Janssen Scientific Affairs, LLC.

Bibliographic details

PubMedID
18954497

DOI
10.1185/03007990802490512

Original Paper URL
http://informahealthcare.com/doi/abs/10.1185/03007990802490512

Indexing Status
Subject indexing assigned by NLM

MeSH
Administration, Oral; Antipsychotic Agents /economics /therapeutic use; Female; Health Expenditures; Humans; Male; Medicaid; Medicare; Models, Theoretical; Randomized Controlled Trials as Topic; Schizophrenia /drug therapy /economics; United States; United States Department of Veterans Affairs

AccessionNumber
22009101239

Date bibliographic record published
09/09/2009

Date abstract record published
19/05/2010