Cost-effectiveness analysis of solifenacin versus oxybutynin immediate-release in the treatment of patients with overactive bladder in the United Kingdom

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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 evaluated the cost-effectiveness of solifenacin compared with oxybutynin immediate-release for treating overactive bladder. The authors concluded that the solifenacin was cost-effective in their baseline analysis, but that remaining uncertainty meant that the results should be interpreted with caution. The study excluded most of the potential treatments for overactive bladder. There remained significant uncertainty in the model parameters, methodology and structure; this is appropriately reflected in the authors’ conclusions.

Type of economic evaluation
Cost-utility analysis

Study objective
The study evaluated the cost-effectiveness of solifenacin compared with oxybutynin immediate-release for treating overactive bladder.

Interventions
Solifenacin (5mg/day with possible titration up to 10mg/day at eight weeks) was compared with immediate-release oxybutynin (5mg three times daily). It was assumed that both drugs would achieve clinical efficacy by eight weeks. Patients of both treatments could discontinue treatment during the first eight weeks. It was assumed that 63% of patients discontinuing treatment would be treated with tolterodine (4mg/day) and the remaining 35% would have no further treatment.

Location/setting
UK/Primary Care.

Methods
Analytical approach:
A previously published decision analytic tree model (Kobelt et al. 1998, see Other publications of related interest) was used to model overactive bladder using published trials and observational data from a UK database. The model had six states relating to five levels of overactive bladder severity and one for drop-out. The model time horizon was one year, consisting of 13 four week cycles. The perspective was that of the UK National Health Service (NHS).

Effectiveness data:
The primary effectiveness data were the number of micturitions/day and leakages/day which informed transition probabilities between disease severity states in the model for the first two cycles of the model. State transitions were from the VECTOR study, which was a randomised controlled trial of the treatments in this analysis (Herschorn et al. 2010, see Other Publications of Related Interest). In the final 11 cycles of the model, patients were allowed to discontinue treatment, but not to move between disease severity states. Discontinuation rates came from the VECTOR study in the first two cycles and from a UK database study for the final 11 cycles.

Monetary benefit and utility valuations:
Utility values came from a published Swedish willingness-to-pay study that used regression analysis to determine how overactive bladder affected utility scores. Utility for second-line therapy and discontinuation was assumed to be the average of all states at baseline.
Measure of benefit:
The summary measure of benefit was quality-adjusted life-years (QALYs).

Cost data:
Costs included general practitioner and outpatient visits based on service assumptions. Incontinence pads use was defined by health state and from a published study for first-line treatment; this was assumed to be identical to weighted mean VECTOR trial baseline for second-line treatment and discontinuation. Drug costs were obtained from the British National Formulary (BNF). All costs were reported in 2010 UK £ and inflated where necessary using the Consumer Price Index.

Analysis of uncertainty:
Key parameters in the model were varied using one-way and scenario sensitivity analyses.

Results
Results were presented with and without the inclusion of incontinence pad costs; the authors stated that true costs were likely to fall somewhere within this range. Costs with pads were £504.30 for solifenacin and £414.14 for immediate-release oxybutynin. A larger proportion of costs was due to pad use for oxybutynin (35.2%) than with solifenacin (22.6%). The baseline incremental cost-effectiveness ratio (ICER) for solifenacin compared with oxybutynin was £7,921/QALY when pads included and £10,705/QALY without pads.

Sensitivity analyses indicated that the model was most sensitive to long-term adherence with the ICER for solifenacin becoming less favourable as adherence increased for oxybutynin, and to assumptions about reasons for discontinuation. Oxybutynin was dominant (it was more effective and less costly) if patients discontinued because they no longer needed further treatment; the ICER for solifenacin was £1,111/QALY if patients discontinued due to adverse events or lack of efficacy.

Authors’ conclusions
The authors concluded that the solifenacin was cost-effective in their baseline analysis, but that remaining uncertainty meant that the results should be interpreted with caution.

CRD commentary
Interventions:
The treatments for overactive bladder were included in the model were clearly defined. However, the authors acknowledged that there were formulations of oxybutynin and tolterodine (and additional potential agents) that were not compared in the model. It was not completely clear which drug would normally be prescribed in the study setting; standard practice should be an essential comparator for local decision-making. Given the large number of alternative treatments available, the assumption of no further treatment options after the failure of second-line therapy may not be realistic.

Effectiveness/benefits:
The authors chose the VECTOR trial to inform transitions in the model because it directly compared oxybutynin and solifenacin. A mixed-treatment meta-analysis, including both direct and indirect evidence for all potential treatments would have been more appropriate for deriving treatment effectiveness. The authors stated that there were several transitions within the model that were assumed to have a zero probability due to no events occurring in the VECTOR trial; it was unclear whether these assumptions were realistic, as a lack of events may be a factor of the VECTOR trial's small sample and short duration. The model also assumed that patients could not transition between health states in second-line therapy and after treatment discontinuation; the basis for this was unclear.

The utility measurement tool was not stated. Several key parameters in the model were based on assumptions. It was unclear whether the assumptions were justified and whether all assumptions were tested in sensitivity analyses.

Costs:
Costs appeared to have been generally derived from appropriate sources. The price year was clearly stated and methods of cost inflation were referenced. Resource use for general practitioner and outpatient visits were assumed; the validity of these assumptions may not be applicable to all settings.
Analysis and results:
The analysis of uncertainty was limited. Many parameters in the model were not varied, and the one-way and scenario sensitivity analyses gave no clue as to the likelihood of any result. A full probabilistic sensitivity analysis using Monte Carlo simulation would have to evaluate uncertainty would have been useful. The results were clearly reported.

The authors conducted a thorough discussion, comparing their work to that of others and acknowledging the limitations of their model and its remaining uncertainty.

Concluding remarks:
The study excluded most of the potential treatments for overactive bladder. There remained significant uncertainty in the model parameters, methodology and structure; the authors' conclusions appropriately reflected this.

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