Colistimethate sodium powder and tobramycin powder for inhalation for the treatment of chronic Pseudomonas aeruginosa lung infection in cystic fibrosis: systematic review and economic model

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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 well-reported study evaluated clinical and cost-effectiveness of colistimethate sodium dry powder for inhalation and nebulised tobramycin for the treatment of chronic Pseudomonas aeruginosa lung infection in patients with cystic fibrosis. The authors concluded that, depending on its price per dose, colistimethate sodium dry powder for inhalation could be less effective and more costly (dominated by) than nebulised tobramycin or it could be cost-effective. The study methods were appropriate and the authors’ conclusions appear appropriate.

Type of economic evaluation
Cost-utility analysis

Study objective
The clinical and cost-effectiveness of colistimethate sodium dry powder for inhalation (DPI) and nebulised tobramycin were evaluated for the treatment of chronic Pseudomonas aeruginosa lung infection in patients with cystic fibrosis.

Interventions
Colistimethate sodium dry powder for inhalation was compared with nebulised tobramycin.

Location/setting
UK/Secondary care.

Methods
Analytical approach:
The cost-effectiveness analysis used a state-transition model, which was developed to simulate the transition between different forced expiratory volume (FEV) states. Data to inform the model came from published literature. The analysis adopted an NHS perspective over a lifetime horizon. A short term (24 week within-trial timeframe) analysis was also undertaken, which required no extrapolation of data.

Effectiveness data:
The main treatment effectiveness data were the probability of moving between forced expiratory volume states and the probability of lung flare-ups (exacerbations). Additional medical history data included the probability of transplantation and mean survival. The treatment effectiveness data came from one clinical trial. The probability of a lung transplant was from the CF Registry and the US Cystic Fibrosis Foundation. The mean survival data came from a multi-centre cohort study; several survival curves were fitted and the best fit selected (Weibull). Several assumptions on the independence of transitions between states and stability of measurements were necessary for modelling. These were fully reported.

Monetary benefit and utility valuations:
The utility values for the different forced expiratory volume strata, exacerbations, and minor and major exacerbations were obtained from the literature.

Measure of benefit:
The measure of benefit was quality-adjusted life-years (QALYs) gained. Total QALYs were calculated as the total time spent in each health state weighted by the respective utility for that health state, less any QALY losses resulting from exacerbations. The measure of benefit was discounted at a rate of 3.5%.

Cost data:
Costs included in the model were those of drug acquisition, nebulisers and management of exacerbations. The prices of the drugs were obtained from the manufacturer. The cost of hospitalisation treatment for came from the 2010-2011 NHS Reference Costs; asthma complications were used as a proxy. The cost of nebulisers was based on expert opinion. Costs were reported in UK £. The price year was 2011. Costs were discounted at a rate of 3.5%.

Analysis of uncertainty:
A probabilistic sensitivity analysis was conducted. Uncertainty in every parameter was accounted for simultaneously and characterised in the cost-effectiveness results. Additional one-way sensitivity analyses were conducted changing parameter estimates because of uncertainty in their validity or structural impact.

Results
Colistimethate sodium dry powder for inhalation resulted in an expected loss of 0.13 QALYs over a patient's lifetime compared with nebulised tobramycin.

When priced higher than nebulised tobramycin, colistimethate sodium dry powder for inhalation was more costly than nebulised tobramycin and was dominated (it was less effective and more costly than nebulised tobramycin).

When colistimethate sodium dry powder for inhalation was priced at £10.60 per dose, the incremental cost-effectiveness ratio for nebulised tobramycin was £50,000; when it was priced at £9.11 per dose, the incremental cost-effectiveness ratio was £126,000.

For the within-trial analysis, colistimethate sodium dry powder for inhalation was only slightly less effective than nebulised tobramycin (0.002 QALYs). The results of the two models (short-term and long-term) appeared consistent.

Authors' conclusions
The authors concluded that the cost-effectiveness of colistimethate sodium dry powder for inhalation varied from being dominated by nebulised tobramycin to being cost-effective depending on its price.

CRD commentary
Interventions:
Two of several possible interventions were included in the analysis. The authors justified the exclusion of the other interventions. Usual practice was included, which would be useful for local decision-makers.

Effectiveness/benefits:
It appeared that the best available evidence was used for the analysis. A systematic review was undertaken and full details were presented. The treatment effectiveness parameters came from a relevant clinical trial. Key modelling assumptions were discussed and justified. Extensive sensitivity analysis was undertaken and the results fully presented and explored. The health outcomes were appropriately captured in the model.

Costs:
The relevant costs for the study perspective were included. The cost estimates were all relevant for the study setting. There was some uncertainty around a couple of estimates and these were appropriately varied in sensitivity analysis. The cost estimates were generally well reported.

Analysis and results:
The analysis was well reported and appeared appropriate. The results were well reported. Uncertainty in the cost-effectiveness analysis was thoroughly evaluated. The authors discussed the strengths and uncertainties of the analysis.

Concluding remarks:
The study methods were appropriate, the study was well reported, and the authors' conclusions appear appropriate.
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