Cost-effectiveness analysis of roflumilast/tiotropium therapy versus tiotropium monotherapy for treating severe-to-very severe COPD

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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 examined the cost-effectiveness of roflumilast with tiotropium versus tiotropium alone for the management of patients with severe-to-very severe chronic obstructive pulmonary disease (COPD), from the perspective of the US payer. The authors concluded that the addition of roflumilast to tiotropium was cost-effective for these patients. The methods were valid and transparent and key areas of uncertainty were considered. The authors’ conclusions appear to be robust.

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

Study objective
This study examined the cost-effectiveness of roflumilast with tiotropium versus tiotropium alone for the management of patients with severe-to-very severe chronic obstructive pulmonary disease (COPD).

Interventions
Combination therapy of oral roflumilast with tiotropium was compared with tiotropium monotherapy.

Location/setting
USA/secondary care.

Methods
Analytical approach:
The analysis was based on a Markov cohort model with time horizons of five years (base case) and 30 years. The authors stated that the perspective of the US payer was adopted.

Effectiveness data:
The clinical inputs were from published literature. The decline in lung function measured by the forced expiratory volume in one second (FEV1) was from published randomised, double-blind, placebo-controlled, multicentre trials. The key input for the analysis was the relative risk reduction in the rate of exacerbation with combined therapy compared with tiotropium alone. These data were from two head-to-head randomised controlled trials of patients with severe and very severe COPD. The long-term progression of disease after the end of the trials, which lasted six months or one year, was assumed.

Monetary benefit and utility valuations:
The utility values were from a study that used the European Quality of life (EQ-5D) questionnaire to elicit patient preferences for the conditions of severe COPD and exacerbations.

Measure of benefit:
Life-years, quality-adjusted life-years (QALYs), all exacerbations avoided, and severe exacerbations avoided were the summary benefit measures. A 3% annual discount rate was applied.

Cost data:
The economic analysis included the costs for COPD maintenance without exacerbations, mild or moderate
exacerbations, and severe exacerbations. These costs were from US published studies and administrative claims, with multipliers for disease severity from a Spanish study. The costs of end-of-life care were from a published source and the drug costs were based on their average wholesale prices. All costs were in $ and were discounted at an annual rate of 3%.

Analysis of uncertainty:
Several model inputs were varied in a one-way sensitivity analysis to identify the most influential parameters. A probabilistic sensitivity analysis was carried out to evaluate the impact of simultaneously varying multiple model parameters. Conventional probability distributions were used and cost-effectiveness acceptability curves were generated.

Results
Over five years, the projected total exacerbations were 8.459 with monotherapy and 6.379 with combination therapy. The severe exacerbations were 0.845 with monotherapy and 0.636 with combination therapy. The life-years were 3.837 with monotherapy and 3.842 with combination therapy. The QALYs were 2.361 with monotherapy and 2.438 with combination therapy. The expected costs were $138,991 with monotherapy and $140,217 with combination therapy.

Compared with monotherapy, the incremental cost with combination therapy was $589 per exacerbation avoided, $5,869 per severe exacerbation avoided, $220,673 per life-year gained, and $15,815 per QALY gained. Over 30 years, the incremental cost was $962 per exacerbation avoided, $8,674 per severe exacerbation avoided, $45,040 per life-year gained, and $16,351 per QALY gained.

The sensitivity analysis showed that the most influential input was the relative risk of exacerbations. Other sensitive parameters were the costs of exacerbations, the time horizon, the decline in FEV1, and the health state utilities. At a threshold of $50,000 per QALY, 70% of simulations found combination therapy to be cost-effective and at $100,000 per QALY this was nearly 100%.

Authors’ conclusions
The authors concluded that the addition of roflumilast to tiotropium was cost-effective for patients with severe-to-very severe COPD.

CRD commentary
Interventions:
The authors justified their selection of the comparators, which appear to have been appropriate for these patients.

Effectiveness/benefits:
No systematic review was reported to identify the relevant sources of evidence. Most of the data were from head-to-head randomised trials, which should have ensured their validity. The authors acknowledged that the data were from studies carried out in various settings, which might not have been comparable, and the relative risk of exacerbations was a secondary outcome from a trial with a small sample. Extensive sensitivity analyses were carried out to overcome these limitations. Assumptions for the long-term data, generally, did not favour the combined therapy. Several benefit measures were used to assess the impact of the therapies on the patients’ health; life-years and QALYs will allow comparisons with the benefits of other interventions.

Costs:
The categories of costs reflected the perspective of the third-party payer as stated. Typical US sources were used for the resource quantities and costs and a clear breakdown of cost items was provided. The authors relied on a Spanish study for the multipliers of severity of disease, but conservative estimates were made. The costs were varied using appropriate distributions in both the univariate and probabilistic sensitivity analyses. Details, such as the price year and discount rate, were provided.

Analysis and results:
The results were extensively presented. An incremental approach was used to combine the costs and benefits of the two approaches. The uncertainty was satisfactorily investigated, using both deterministic and probabilistic approaches, and the methods and results were clearly described. The authors acknowledged some of the potential limitations to their
analysis. They stated that this was the first study conducted in the US to compare combined therapy against tiotropium monotherapy, and the external validity of their findings might be low. More clinical trials were needed to corroborate the results.

Concluding remarks:
The methods were valid and transparent and key areas of uncertainty were considered. The authors’ conclusions appear to be robust.

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