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 etanercept combined with methotrexate, followed by a dose reduction, for patients with early active rheumatoid arthritis. The authors concluded that this combination and dose reduction, compared with methotrexate alone, was cost-effective. The study was well conducted and reported; the results should be considered with the limitations presented.

Type of economic evaluation
Cost-utility analysis

Study objective
This study examined the cost-effectiveness of etanercept combined with methotrexate, followed by a dose reduction, for patients with early active rheumatoid arthritis.

Interventions
The interventions were etanercept combined with methotrexate, and methotrexate alone. In the combination, the dose of etanercept was reduced to half for those patients in remission.

Location/setting
Sweden/secondary care.

Methods
Analytical approach:
The analysis used a published Markov model with a 10-year horizon. This published model for a severe rheumatoid arthritis population was adapted to represent an early rheumatoid arthritis population. It had five health states based on functional capacity. The transitions between states occurred every six months. A reduction in the dose of etanercept was possible for patients with a disease activity score (DAS28) of less than 2.6 for two consecutive six-month cycles. The authors stated that the perspective of society was adopted.

Effectiveness data:
The clinical data came from various sources, including a randomised controlled trial comparing the combination against methotrexate alone for early rheumatoid arthritis. This Combination of Methotrexate and Etanercept in active early rheumatoid arthritis (COMET) trial supplied the treatment effectiveness. The South Swedish Arthritis Treatment Group (SSATG) registry provided the effectiveness of the second biologics and their impact on functional capacity (Health Assessment Questionnaire, HAQ, score) and DAS28. The impact of a reduced dose of etanercept came from a cohort study (PADOVA). The key model inputs were the change in HAQ score, the change in DAS28, the efficacy of dose reduction, and the percentage of patients switching at discontinuation.

Monetary benefit and utility valuations:
The utility values were derived from a survey of the population in Southern Sweden, using the European Quality of life (EQ-5D) questionnaire.

Measure of benefit:
Quality-adjusted life-years (QALYs) were the summary benefit measure and they were discounted at 3% per annum.
Cost data:
The analysis considered the health care costs, community services, patient costs, and productivity losses. The resource data came from the population survey that provided the utility data. All costs were presented in Euros (EUR) for the year 2008 and a 3% annual discount rate was applied.

Analysis of uncertainty:
A probabilistic sensitivity analysis, using 300,000 simulations, was carried out. The key inputs that were varied in the deterministic sensitivity analysis were the time horizon, the perspective, the discontinuation rate, the proportion of patients switching or returning to full dose, and the utility score.

Results
In the base case, over 10 years, the total costs for the combined etanercept/methotrexate strategy were EUR 170,800 and the total QALYs were 5.30. The total costs for methotrexate alone were EUR 155,300 and the total QALYs were 4.15.

The cost per quality-adjusted life-year (QALY) gained with the combination compared with methotrexate alone was EUR 13,500.

The deterministic sensitivity analysis showed that the results were sensitive to varying the time patients remained on half dose and the perspective. Over a longer 20-year time horizon, the cost per QALY gained was EUR 8,200. The probabilistic sensitivity analysis showed that the combination was cost-effective in all simulations when the willingness-to-pay threshold was greater than EUR 20,000.

Authors’ conclusions
The authors concluded that etanercept combined with methotrexate, followed by dose reduction for patients achieving remission, was cost-effective.

CRD commentary
Interventions:
The selection of the comparators seems to have been appropriate, but it was not clear if the results were valid for all biologic therapies in this population or just etanercept. If they only apply to etanercept, other biologics in combination with methotrexate could have been included as comparators.

Effectiveness/benefits:
The clinical data were from a selection of relevant studies. Efficacy was mainly from a randomised controlled trial, and this design should have ensured the validity of these clinical estimates. Other data, such as the efficacy of dose reduction, came from a cohort study and authors’ assumptions, which may be less reliable. The methods of the studies that supplied the clinical data were not well described, making it difficult to fully assess the internal validity of the data or to be sure that all the relevant data were included. The use of QALYs was appropriate, as this measure not only captures the impact of the interventions on quality of life, but also allows cross-disease comparisons to be made.

Costs:
The perspective of the analysis was reported and it appears that all relevant cost categories considered. Detailed cost items were not reported, but further details were reported to be available online; some unit costs were presented. This reduces the transparency of the analysis. The sources for the resource use estimates were appropriately reported and appear to have been representative of and relevant to Sweden. Other details, such as the price year and discounting, were reported.

Analysis and results:
Full details of the model structure and methods were presented. An incremental approach was appropriately used to combine the costs and benefits and sensitivity analyses were satisfactorily conducted. The findings were fully reported and discussed. The authors highlighted some limitations of their analysis and identified areas, such as the criteria for dose reduction that required additional research. Supplemental data files were available on the Internet.

Concluding remarks:
The study was well conducted and reported; the results should be considered with the limitations presented.

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