Cost-effectiveness of abatacept in patients with moderately to severely active rheumatoid arthritis and inadequate response to tumor necrosis factor-alpha antagonists


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 cost-effectiveness of abatacept for the treatment of women aged 55 to 64 years with moderately to severely active rheumatoid arthritis and inadequate response to tumour necrosis factor-α antagonists. The authors concluded that abatacept in addition to disease-modifying antirheumatic drugs (DMARDs) was a cost-effective alternative to oral DMARDs alone. The methodology appears to have been valid, which should ensure that the authors’ conclusions are robust.

Type of economic evaluation
Cost-utility analysis

Study objective
The objective was to examine the cost-effectiveness of abatacept for the treatment of women aged 55 to 64 years with moderately to severely active rheumatoid arthritis and inadequate response to tumour necrosis factor-α antagonists.

Interventions
Abatacept added to oral disease-modifying antirheumatic drugs (DMARDs) was compared with oral DMARDs alone. Patients received abatacept at a dose between 500mg and 1,000mg depending on body weight on day one, day 14, day 29, and every four weeks thereafter.

Location/setting
USA/secondary care.

Methods
Analytical approach:
The analysis was based on a simulation model that depicted the progression of disability assessed by the Health Assessment Questionnaire Disability Index (HAQ-DI). The model used both 10-year and lifetime horizons. The authors stated that the perspective of the third-party payer was adopted.

Effectiveness data:
The clinical data came from a selection of known, relevant studies. Most of the evidence on the treatment effect and safety was derived from a double-blind, placebo, randomised controlled trial (RCT); the Abatacept Trial in Treatment of Anti-TNF Inadequate Responders (ATTAIN). This trial included 258 patients, who received abatacept or placebo for six months in addition to their stable dosage of oral DMARDs. Other clinical inputs came from published studies, which were mainly observational and assessed the disease progression over time. The key clinical input was the efficacy of abatacept. Some assumptions were also required.

Monetary benefit and utility valuations:
The utility values were estimated from published data, which used the European Quality of life (EQ-5D) questionnaire Weighted Health Index, and the HAQ-DI with about 19,000 people who had rheumatoid arthritis.

Measure of benefit:
Quality-adjusted life-years (QALYs) were the summary benefit measure and were discounted at an annual rate of 3%.
Cost data:
The economic analysis included the costs of medications (acquisition, administration, and monitoring) and all other direct medical care services (in-patient and out-patient). The quantities of resources associated with the medical services were assumed to vary with variations in the HAQ-DI. The costs were estimated using product labels, published guidelines, and Medicare reimbursement rates. All costs were in US dollars ($) and a 3% annual discount rate was applied. The price year was 2006.

Analysis of uncertainty:
First- and second-order Monte Carlo simulations were undertaken on all the model inputs and 95% confidence intervals (CIs) around the model outcomes were generated. A deterministic sensitivity analysis was also carried out on the model inputs, such as therapy discontinuation rate, timing of therapy discontinuation, relationship between HAQ-DI and mortality, improvements in mortality associated with abatacept, expected rate of disease progression, and threshold for clinically meaningful improvement in the HAQ-DI. Various age cohorts were considered and the analysis was also replicated for men.

Results
Over 10 years, the discounted QALYs were 2.7 with oral DMARDs alone and 3.6 with abatacept. The costs were $55,151 with oral DMARDs alone and $100,648 with abatacept. The incremental cost per QALY gained with abatacept was $50,576 (95% CI 47,056 to 54,944).

Over the patient lifetime, the discounted QALYs were 3.4 with oral DMARDs alone and 4.7 with abatacept. The costs were $82,489 with oral DMARDs alone and $140,714 with abatacept. The incremental cost per QALY gained with abatacept was $45,979 (95% CI 42,678 to 49,932).

The simulation showed that the probability that abatacept was cost-effective was 100% at a threshold of $100,000 per QALY, 0% at a threshold of $20,000 per QALY, and 39% at a threshold of $50,000 over a 10-year time horizon. The probability of being cost-effective was 100% over patient lifetime at a threshold of $50,000 per QALY.

In all sensitivity analyses, the incremental cost-utility ratio ranged from $43,443 to $80,673 over a 10-year time horizon and from $40,836 to $70,419 over a patient lifetime horizon. The most influential model inputs were the thresholds for HAQ-DI and assumptions about therapy discontinuation. Variations in other inputs did not produce substantial changes in the base-case findings.

Authors' conclusions
The authors concluded that abatacept in addition to DMARDs was a cost-effective alternative to oral DMARDs alone.

CRD commentary
Interventions:
The authors justified their selection of the comparators. DMARDs alone were an appropriate alternative given that the objective was to examine the net value of abatacept. The authors stated that, at the time of the study, no data were available for rituximab nor for the use of a second tumour necrosis factor-α antagonist after the failure of the first one.

Effectiveness/benefits:
The data sources were selected, which assumes that the authors were aware of the most appropriate sources for the clinical inputs. A RCT is generally considered to be a valid source of evidence, especially for the efficacy of therapy and the double-blind design further improves the internal validity of these inputs. Other data came from sources that were mainly observational and assessed the long-term progression of the disease. The issue of uncertainty was extensively investigated in the sensitivity analysis. The authors did not consider the problem of heterogeneity of data, which was relevant given the use of multiple sources, with potentially different patient populations and types of intervention. The derivation of the utility values appears to have been appropriate and used a validated instrument. QALYs are a valid benefit measure given the impact of the disease on both survival and quality of life.

Costs:
The categories of costs were consistent with the perspective and were extensively described, especially for the
medication cost, which included details on unit costs, dosages, and monitoring expenses. Other costs were reported as macro-categories related to the disability stage of the disease. This approach is quite common for rheumatoid arthritis patients, but it limits the transparency of the analysis. The data sources, use of discounting, and price year were clearly reported. Potential variations in the cost estimates were considered in the sensitivity analysis.

Analysis and results:
The incremental approach used to synthesise the costs and benefits was appropriate and both discounted and undiscounted results were reported. The issue of uncertainty was satisfactorily investigated using various approaches, which confirmed that the base-case findings were robust. The decision model was extensively described, with transition patterns, and diagrams were given. The model focused on women aged 55 to 64 years, but the results were similar for other age groups and for men.

Concluding remarks:
The methodology appears to have been valid, which should ensure that the authors' conclusions are robust.

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