Biologic drugs for rheumatoid arthritis in the Medicare program: a cost-effectiveness analysis

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 assessed the cost-effectiveness of four biological drugs, covered by Medicare in the USA, for the treatment of rheumatoid arthritis. The authors concluded that etanercept or adalimumab should be preferred to infliximab as the first-line biological agent for the treatment of rheumatoid arthritis within the Medicare programme. The quality of the study methodology was good in terms of the sources used, statistical methods applied and reporting of data and results. This enhances the validity of the authors’ conclusions. However, the issue of drug wastage with infliximab should have been considered in order to fully estimate the relative cost-effectiveness of biological agents.

Type of economic evaluation
Cost-utility analysis

Study objective
The objective was to assess the cost-effectiveness of four biological drugs, covered by Medicare in the USA, for the treatment of rheumatoid arthritis.

Interventions
The four biological drugs included in the analysis were etanercept, adalimumab, infliximab and anakinra. Recommended doses were used: 50 mg/week for etanercept, 40 mg every other week for adalimumab and 100 mg/day for anakinra. Infliximab was initially given at a dose of 3 mg/kg at week 0, 2, 6 and then every 8 weeks, but an increase in dose (up to a maximum of 10 mg/kg) was assumed.

Location/setting
USA/secondary care.

Methods
Analytical approach:
A decision model based on patient-level simulations was developed in order to estimate the lifetime costs and quality of life associated with the four biological agents. The time horizon of the analysis was lifetime. The authors stated that the perspective of Medicare was adopted in the study.

Effectiveness data:
The clinical data were obtained from a selection of known relevant studies. Two sources in particular were used. First, treatment effect in the short term was based on a meta-analysis of 13 randomised clinical trials (RCTs); a meta-regression was also conducted to take differences among the RCTs into consideration. Second, long-term disease progression was based on longitudinal database of patient self-reported data (the National Databank of Rheumatic Diseases, NDB). This included 1,490 patients for etanercept, 1,403 for infliximab, 74 for anakinra and 160 for adalimumab. The key clinical outcome was the impact of biological drugs based on the American College of Rheumatology 20% or 50% improvement criteria.

Monetary benefit and utility valuations:
Utility weights were derived from a US population, on the basis of the EuroQol (EQ-5D) Index in the NDB.

Measure of benefit:
The summary benefit measure was the quality-adjusted life-years (QALYs). These were calculated by associating utility weights with the scores of the Disability Index of the Health Assessment Questionnaire. The QALYs were discounted at an annual rate of 3%.

Cost data:
The categories of costs included in the analysis were biological drugs, physician visits, other medications, hospitalisations, radiographs and laboratory work. Resource use was based on data derived from the NDB. The unit costs were derived from the Centers for Medicare and Medicaid Services using published methodology. Future costs were discounted at an annual rate of 3%. The price year might have been 2005. The costs were in US dollars ($).

Analysis of uncertainty:
A probabilistic sensitivity analysis was carried out in order to deal with the issue of uncertainty. Each model input was assigned a probabilistic distribution and cost-effectiveness acceptability curves were generated. In addition, a one-way sensitivity analysis was used to explore alternatives to the base-case scenario, with data derived from practice rather than from RCTs.

Results
The mean cost per patient was $94,029 with infliximab, $81,181 with etanercept, $79,535 with adalimumab and $50,608 with anakinra.

The mean QALYs per patient were 7.64 with infliximab, 7.66 with etanercept, 7.64 with adalimumab and 7.44 with anakinra.

The incremental analysis showed that anakinra was the least effective. As it was less effective than current practice it was not considered a relevant option.

Infliximab was dominated by both etanercept and adalimumab since it provided similar QALYs at higher costs.

In comparison with adalimumab, the incremental cost per QALY gained with etanercept was $92,058, while in comparison with anakinra, the incremental cost per QALY gained with adalimumab was $142,726. Anakinra was thus excluded from further analysis because of its lower effectiveness.

The cost-effectiveness acceptability curve showed that, at a willingness-to-pay of zero for a QALY, the optimal strategy was adalimumab in 61% of simulations (39% for etanercept).

The two treatments had a similar likelihood of being cost-effective at a willingness-to-pay threshold of $110,000. Infliximab was not cost-effective even at high thresholds of willingness-to-pay.

The deterministic sensitivity analysis confirmed the base-case findings. However, there was one case where infliximab was more cost-effective than the other options, namely, when dose increase was not considered and infliximab was given constantly at the same dosage.

Authors' conclusions
The authors concluded that etanercept or adalimumab would be preferable to infliximab as the first-line biological agent for the treatment of rheumatoid arthritis within the US Medicare programme.

CRD commentary
Interventions:
The rationale for the selection of the comparator was clear. The authors justified the exclusion of two newer biological agents (abatacept and rituximab) that were not covered by the payer. Dosages were reported in full. These drugs are also likely to be relevant in other health care systems.

Effectiveness/benefits:
The clinical estimates appear to have been derived from valid sources. The use of a meta-analysis of clinical trials to
estimate the short-term treatment effect, and that of an observational study to model disease progression, represent a valid approach. In addition, since no head-to-head comparisons of the selected drugs were available, the authors performed a meta-regression to take account of the heterogeneity in patient populations and treatment received among clinical trials. Overall, details of the derivation of model inputs from published studies were extensively presented and discussed. In general, the clinical analysis appears to have been robust and valid given the good reporting of the methodology used. The use of QALYs represents the most appropriate measure of benefit for rheumatoid arthritis.

Costs:
The analysis of the costs was consistent with the viewpoint of the analysis. The categories of costs included in the analysis were reported, as were other key details on resource consumption, sources of data, price year, discounting and use of statistical methods. The use of patient co-payments was reported. However, there were few details on a key element of cost for infliximab, namely drug wastage. Since infliximab is administered on the basis of a 3-mg/kg dose and 100-mg vials are available, assumptions about drug wastage appear fundamental to determining the total drug cost.

Analysis and results:
The costs and benefits were combined appropriately. The results of both the base-case and the sensitivity analysis were presented clearly. The issue of uncertainty was appropriately addressed by means of both deterministic and probabilistic sensitivity analyses. Clear details of the probabilistic approach used in the analysis were given. Overall, the conduct of the analysis appears to have been consistent with the scope of the study. However, different assumptions about drug wastage for infliximab could have changed the results of the analysis, with infliximab becoming more cost-effective than other drugs.

Concluding remarks:
On the whole, the study methodology seems appropriate and was reported clearly. The authors’ conclusions appear valid and robust.

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**Other publications of related interest**


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