The cost-effectiveness of infliximab in the treatment of ankylosing spondylitis in Spain: comparison of clinical trial and clinical practice data

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 study assessed the cost-effectiveness of infliximab for the treatment of ankylosing spondylitis (AS). The authors concluded that infliximab was a cost-effective treatment from the perspectives of society (a dominant strategy) and the health care system in Spain. In general, the study appears to have been based on valid methodology and a transparent description of the model and sources of data was given. Although a more extensive sensitivity analysis would have been useful, the authors’ conclusions appear to be valid.

Type of economic evaluation
Cost-utility analysis

Study objective
The objective was to assess the cost-effectiveness of infliximab for the treatment of ankylosing spondylitis (AS).

Interventions
Infliximab (5mg/kg every six weeks) was compared with no treatment. A dosage of 5mg/kg every eight weeks was considered in a secondary analysis.

Location/setting
Spain/secondary care.

Methods
Analytical approach:
This economic evaluation was based on a published decision model (a standard decision tree plus a Markov model) which was adapted to the Spanish setting using country-specific data. The time horizon of the study was 40 years. The authors stated that the perspectives of society and the health care system were adopted.

Effectiveness data:
The clinical data were derived from published studies which were selected by the authors. The effectiveness data were obtained from two sources. In the first analysis, the data were derived from an international double-blind, placebo-controlled, 12-week, clinical trial with open (double-blind removed) extension in 70 patients with confirmed AS and active disease who were followed up for 102 weeks. In the second analysis, the data were retrieved from an open, multicentre, clinical trial in Spain with 42 patients who were followed up for 60 weeks. The data on disease progression were obtained from a sample of 1,110 patients who responded to postal surveys at the University of Bath in the UK. Some key assumptions on treatment discontinuation and the long-term efficacy of treatment were necessary, given the lack of long-term data.

Monetary benefit and utility valuations:
The utility valuations were derived from a cross-sectional retrospective survey of 601 randomly selected AS patients in Spain, using the EQ-5D questionnaire. When data from these Spanish patients were not available, or when there were insufficient data to populate some health states, data from a larger cohort of 1,413 UK patients were used.

Measure of benefit:
Quality-adjusted life-years (QALYs) were the summary benefit measure used and a 3% annual discount rate was
applied.

Cost data:
The three main cost categories considered were direct health care costs, non-medical direct costs associated with informal care, and indirect costs related to productivity losses. The cost of infliximab also included the management of adverse events. Resource consumption was derived from the previously mentioned cross-sectional retrospective survey using a validated questionnaire. The costs for health care services were valued using public sources. For example, the cost of infliximab was based on the official list price. Informal care was valued using the replacement approach, while productivity losses were calculated using the human capital method. All costs were in Euros (EUR) and the price year was 2005. Given the long-term horizon of the analysis, costs accrued after the first year were discounted at an annual rate of 3%.

Analysis of uncertainty:
A deterministic sensitivity analysis was carried out by varying specific model inputs such as discount rate, discontinuation rate, time horizon, and disease-specific mortality. Given the lack of definitive data on treatment progression in the long-term, the results were presented for three scenarios which were no worsening of Bath AS functional index (BASFI) while on treatment, no effect of treatment on BASFI, and half the natural rate of progression.

Results
From a societal perspective, infliximab treatment was dominant (i.e. simultaneously more effective and less expensive than no treatment) in all scenarios.

From the perspective of the health care system, the incremental cost per QALY gained ranged from EUR 5,307 (best case) to EUR 31,721 (worst case) depending on the scenario considered and the source of the data. The incremental cost per QALY was lower when data from the Spanish open trial were used (range from EUR 5,307 to EUR 13,659) than when data from the double-blind clinical trial were used (range from EUR 15,152 to EUR 31,721).

The sensitivity analysis indicated that infliximab almost always remained the dominant strategy from the societal perspective, while the results from the perspective of the health care payer were sensitive to variations in treatment regimen, time horizon, and treatment discontinuation. Specifically, cost-utility ratios above EUR 50,000 per QALY were observed for time horizons shorter than 10 years.

Authors’ conclusions
The authors concluded that infliximab was a cost-effective treatment for AS from the perspectives of both society (dominant strategy) and the health care system in Spain.

CRD commentary
Interventions:
The selection of no treatment as the background comparator reflected the nature of the placebo-controlled trial used to derive the clinical evidence. However, it may not be the most appropriate comparator in other settings.

Effectiveness/benefits:
In order to include the evidence most relevant to the objective, the sources of data were selected from studies known to the authors. The authors justified their selection, which may represent valid studies given their robust design. It was noted that the small sample size of some of these sources might represent a drawback to the study. Some assumptions on treatment effectiveness were made because of a lack of conclusive evidence. These issues tend to enhance the validity of the clinical analysis, which was carried out transparently. The derivation of QALYs was clearly described and reflected the Spanish setting. QALYs are a validated measure of the impact of treatment on patients’ health. Furthermore, they allow for cross-disease comparisons.

Costs:
The analysis of costs was carried out from two perspectives, which makes the findings relevant for different payers. In particular, the inclusion of the cost of informal care represents a positive aspect of the economic analysis, given the
progressive nature of the disease. The authors provided some key details of the calculation of costs, taking into account the correlation with disease severity. The price year and the use of discounting were reported. Furthermore, the methodological approaches used to derive indirect costs were described. However, little information on the sources used was provided, and the authors did not give a detailed breakdown of cost items. This might limit the transparency of the whole economic analysis. The impact of using alternative costs was not investigated.

**Analysis and results:**
The synthesis of costs and benefits was appropriately performed and presented. The issue of uncertainty was only addressed by means of a deterministic sensitivity analysis which was restricted to a few model inputs. However, different scenarios were considered. The authors noted that the model framework required a number of simplifying assumptions, which might make the model less representative. They presented multiple scenarios to try to overcome this limitation of the analysis.

**Concluding remarks:**
In general, the study appears to have been based on a valid methodology and a transparent description of the model and sources of data was provided. Although a more extensive sensitivity analysis would have been useful, the authors’ conclusions appear to be valid.

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