

## NHS Economic Evaluation Database (NHS EED)

### Budget impact model of rituximab after failure of one or more TNFalpha inhibitor therapies in the treatment of rheumatoid arthritis

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CRD summary	The objective was to examine the economic implications of using rituximab for the treatment of rheumatoid arthritis after the failure of one or more tumour necrosis factor (TNF $\alpha$ ) inhibitors. The authors concluded that rituximab led to important cost savings due to its lower drug acquisition cost. The study was based on valid methodology and considered various scenarios. The authors' conclusions appear to be valid.
Type of economic evaluation	Cost-effectiveness analysis
Study objective	The objective was to examine the economic implications of using rituximab for the treatment of severe rheumatoid arthritis in patients who had failed treatment with one or more tumour necrosis factor (TNF $\alpha$ ) inhibitors.
Interventions	Rituximab, used for second and subsequent lines of treatment after the failure of one anti-TNF $\alpha$ treatment, was compared with the following TNF $\alpha$ inhibitors: infliximab, etanercept, and adalimumab. While infliximab and rituximab were always given in combination with methotrexate, etanercept and adalimumab could be given alone or in combination with methotrexate.
Location/setting	France/secondary care.
Methods	<p><u>Analytical approach:</u> A dynamic Markov model with a four-year time horizon was developed to determine the budget impact of the alternative strategies. The authors stated that the analysis was carried out from the perspective of the French health care system.</p> <p><u>Effectiveness data:</u> The clinical data came from published literature, but the approach used to identify the relevant sources of data was not reported. It is likely that only randomised controlled trials were selected for the analysis since the efficacy data were derived from 16 trials. The data were combined using a Bayesian mixed treatment comparison (MTC), with the combination of methotrexate and placebo as the reference comparator. The MTC approach included the assessment of the heterogeneity among the trials. The key clinical endpoint was the level of American College of Rheumatology 20 (ACR20) responders.</p> <p><u>Monetary benefit and utility valuations:</u> Not included.</p> <p><u>Measure of benefit:</u> No summary benefit measure was used. The clinical outcomes of the analysis were the efficacy, safety, and early discontinuation rates.</p> <p><u>Cost data:</u> The economic analysis included the following cost categories: treatment administration, hospitalisations, out-patient visits, concomitant treatments, imaging and tests, and hospital-to-home transport. The dosages and patterns of administration of the study drugs were derived from the summary of product characteristics. The data for the other resources were derived from a multi-centre observational retrospective study carried out between April and July 2006. This included a sample of 293 patients treated at 55 public hospitals and four not-for-profit hospitals. These resources were valued using published diagnosis-related group</p>

	<p>rates and other French national tariffs. All costs were in Euros (EUR) and the price year was not reported.</p> <p><u>Analysis of uncertainty:</u> Three scenarios for rituximab market share were considered. In H1, rituximab was not marketed and the market shares were infliximab 16%, etanercept 38%, and adalimumab 46%. In H2, rituximab was introduced into the market progressively with each failing patient being switched to rituximab and each new patient to second-line biologic treatment starting on rituximab. In H3, rituximab was the only treatment available over the study period. The issue of uncertainty was investigated by focusing on the patterns of resource consumption in different lines of treatment or in patients with various levels of disease severity.</p>
Results	<p>Adalimumab plus methotrexate was the most effective option in terms of ACR20 results, followed by rituximab plus methotrexate, and the difference between these two options was not statistically significant.</p> <p>The total annual cost per patient was EUR 16,555 in scenario H1 (no rituximab) and EUR 11,444 in scenario H3 (rituximab only). In scenario H2, the total direct medical costs decreased progressively to the same level as in scenario H3 at the end of the four-year period.</p> <p>In the whole eligible population (5,700 rheumatoid arthritis patients) over the four years, the total costs were EUR 378 million in scenario H1 and EUR 260 million in scenario H3. Drug acquisition costs accounted for 80% of total costs for the TNF<math>\alpha</math> inhibitors and 65% for rituximab.</p> <p>The sensitivity analysis demonstrated that scenario H3 remained the least expensive.</p>
Authors' conclusions	<p>The authors concluded that rituximab led to important cost savings, if used after the failure of one or more TNF<math>\alpha</math> therapies, due to its lower acquisition cost.</p>
CRD commentary	<p><u>Interventions:</u> The authors justified their selection of the comparators, which were appropriately chosen to include all the relevant treatment strategies for patients with rheumatoid arthritis. A comparison of rituximab with other new biologics such as abatacept or tocilizumab appears to have been beyond the scope of this analysis.</p> <p><u>Effectiveness/benefits:</u> The authors did not report the method used to identify the relevant sources of data, but the use of randomised controlled trials should have ensured the validity of the clinical estimates. The MTC methodology was a valid approach for synthesising the clinical data, as direct head-to-head comparisons were not available. The clinical estimates were used as inputs for the economic model rather than in a comparison of effectiveness among inputs. In general, the clinical analysis was well conducted and the clinical estimates were clearly presented.</p> <p><u>Costs:</u> The analysis of costs reflected the economic viewpoint in terms of the cost categories and their sources. The unit costs and details of resource consumption were not presented separately for all items and the price year was not reported. These issues tend to limit the transparency of the economic analysis. The resource use data were based on a retrospective analysis of patient data, which did not include the patients' subsequent lines of treatment. The use of discounting was not reported and it could have been relevant given the relatively long time frame of the analysis. The cost estimates were treated deterministically.</p> <p><u>Analysis and results:</u> This was a cost-consequences analysis and a synthesis of the costs and benefits was not required. The analysis focused on the economic comparison and the budget impact of introducing rituximab into the French market. The sensitivity analyses investigated the issue of uncertainty, only in terms of resource consumption, using a deterministic approach. The authors compared their findings with those from other studies showing similar results. Extensive information on the decision model was reported and the use of a dynamic approach was a strength of the analysis. The authors acknowledged that the main limitation</p>

	<p>of their analysis was that the resource consumption was identical between the second and subsequent treatment lines.</p> <p><u>Concluding remarks:</u> The study was based on valid methodology and considered various scenarios. The authors' conclusions appear to be valid.</p>
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Other publications of related interest	<p>Cohen SB, Emery P, Greenwald MW, et al. Rituximab for rheumatoid arthritis refractory to anti-tumor necrosis factor therapy: results of a multicenter, randomized, double-blind, placebo-controlled, phase III trial evaluating primary efficacy and safety at twenty-four weeks. <i>Arthritis and Rheumatism</i> 2006; 54: 2793-2806.</p> <p>Kavanaugh A. Is there a pharmacoeconomic argument supporting the use of tumor necrosis factor inhibitors in early rheumatoid arthritis? <i>Nature Clinical Practice. Rheumatology</i> 2006; 2: 346-347.</p> <p>Kobelt G, Eberhardt K, Geborek P. TNF inhibitors in the treatment of rheumatoid arthritis in clinical practice: cost and outcomes in a follow-up study of patients with RA treated with etanercept or infliximab in southern Sweden. <i>Annals of the Rheumatic Diseases</i> 2004; 63: 4-10.</p> <p>Fautrel B, Woronoff-Lemsi MC, Ethgen M, et al. Impact of medical practices on the costs of management of rheumatoid arthritis by anti-TNFalpha biological therapy in France. <i>Joint, Bone, Spine</i> 2005; 72: 550-556.</p>
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