# Economic evaluation of oral valdecoxib versus diclofenac in the treatment of patients with rheumatoid arthritis in a randomized clinical trial

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## 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.

## Health technology

Valdecoxib (20 mg once daily), an oral cyclooxygenase (COX)-2-specific inhibitor, was compared with diclofenac (75 mg twice daily), a non-specific non-steroidal anti-inflammatory drug (NSAID), for the symptomatic treatment of rheumatoid arthritis.

## Type of intervention

Secondary prevention, treatment.

## Economic study type

Cost-effectiveness analysis.

## Study population

The study population comprised all patients who had had at least one dose of study medication. No further details were provided.

## Setting

The setting was secondary care. The economic study was carried out by companies based in the USA. The resource and clinical evidence was derived from a multi-national randomised controlled trial (RCT) that included the UK.

## Dates to which data relate

There was no information about when the effectiveness and resource use data were collected. The costs were expressed in 2000/2001 prices.

## Source of effectiveness data

The effectiveness data were derived from a single study.

## Link between effectiveness and cost data

A prospective costing exercise was carried out on the same sample as that which provided the effectiveness data.

## Study sample

The trial was powered to detect differences in the primary outcomes of the RCT, but not all of the outcomes used in the economic evaluation. The final sample comprised 483 patients, of which 246 were randomised to valdecoxib 20 mg and 237 were randomised to diclofenac 150 mg. No further information on the study sample was provided. The authors referred to Pavelka et al. (see Other Publications of Related Interest).

## Study design

The study was a prospective, double-blind, RCT that was conducted in multiple centres. The study compared oral valdecoxib (20 mg once daily) with diclofenac (75 mg twice daily) for the symptomatic treatment of rheumatoid arthritis. Data were collected for 26 countries and 7% of the sample was derived from the UK. The duration of treatment was 6 months. A smaller proportion of patients treated with valdecoxib withdrew from the trial for any reason compared with those taking diclofenac (19% versus 25%). No further information on the study design was provided. The reader is referred to Pavelka et al. (see Other Publications of Related Interest).

## Analysis of effectiveness

The analysis of the study was conducted on an intention to treat basis. Clinical outcomes included end points for efficacy, safety and tolerability. Efficacy end points included the American College of Rheumatology Responder Index, arthritis pain (visual analogue scale), global assessment of disease (patient and physician), the modified Health Assessment Questionnaire, swollen joint counts, and tender or painful joint counts and scores. Safety end points included the incidence of gastroduodenal ulceration observed by endoscopy at the end of the trial, the incidence of adverse events, and withdrawal due to adverse events. The EQ-5D instrument was used as a measure of quality of life. Although there were differences in baseline demographics, it was unclear whether any adjustments for these differences were made to determine effectiveness.

## Effectiveness results

No statistical differences were found between the arms of the study in any of the primary end points.

No differences in quality of life were detected.

The proportion of patients with endoscopic ulcers at the end of the trial was significantly lower in the valdecoxib group than in the diclofenac group (5.6% versus 16.3%; p<0.001).

## Clinical conclusions

The results of the trial suggested similar effectiveness for both drugs. However, valdecoxib treatment was associated with lower gastrointestinal serious adverse events.

## Measure of benefits used in the economic analysis

As the effectiveness results showed no differences in effectiveness between the arms, the economic analysis was based on cost-differences only. The reader is thus referred to the 'Effectiveness Results' section, reported earlier.

## Direct costs

The direct costs included in the analysis were those of the UK NHS. The information on resource use was obtained from the case form questionnaire, and information collected on concomitant medication, unscheduled outpatient visits (general practitioner, specialist, hospital), hospitalisation) and procedures. No information on the dates when the data were collected was provided. The study was planned to calculate the total cost per patient over the 6-month follow-up and to include the treatment of all adverse events occurring in both treatment groups. Detailed information on resource use was not provided, and the costs were expressed in 2000/2001 prices. The unit cost sources included the Monthly Index of Medical Specialties in the UK (2001 edition) and the NHS for the year 2000. The costs excluded drug acquisition costs, as did the analysis of differences in the costs between the two treatments, because the price of valdecoxib had not been established in the UK at the time of the analysis. The costs were not discounted since the chosen time horizon was 6 months.

## Statistical analysis of costs

The costs were analysed and presented in a stochastic manner. Descriptive statistics, such as means and standard deviations (SDs), were used to present the results of the point estimates. Mean cost-differences (valdecoxib -

diclofenac) and 95% nonparametric confidence intervals (CIs) were calculated to detect significant differences between the groups.

## Indirect Costs
The indirect costs were not included.

## Currency
UK pounds sterling ().

## Sensitivity analysis
As patient level data were available, uncertainty was dealt with through standard classical statistical techniques.

## Estimated benefits used in the economic analysis
See the 'Effectiveness Results' section.

## Cost results
The mean total cost per patient was 334 (SD=720) for the valdecoxib group and 534 (SD=1,428) for the diclofenac group. The difference of -199 (95% CI: -417 - 9) was significant and favoured the valdecoxib arm.

Reductions in costs were achieved for all the categories in the study, and were significantly lower for hospitalisations (-136.30, 95% CI: -275.00 - -16.30) and procedures (-25.24, 95% CI: -48.70 - -5.80).

The mean reduced cost of valdecoxib compared with diclofenac per patient per day was 3.40.

The savings obtained in the valdecoxib group primarily resulted from reduced health-care resource utilisation and a concomitant reduction in costs associated with lower incidence of gastrointestinal serious adverse effects, as shown in the 'Effectiveness Results' section.

## Synthesis of costs and benefits
The costs and effects were not combined as the analysis was considered a cost-minimisation study.

## Authors' conclusions
A significant reduction in health-care resource utilisation with the use of cyclooxygenase (COX)-2-specific inhibitors can be expected, owing to the more favourable upper gastrointestinal safety of these drugs compared with non-specific non-steroidal anti-inflammatory drugs (NSAIDs).

## CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparators was clear. Pfizer's drug was compared with a competitive drug, both of which were compared in a multi-national RCT. The use of NSAIDs is associated with upper gastrointestinal adverse events. The efficacy of COX-2 specific inhibitors and its serious adverse effects versus NSAIDs is still uncertain. You should decide if this is widely used health technology in your own setting.

## Validity of estimate of measure of effectiveness
The authors used an RCT to determine the clinical effectiveness. This design was appropriate for the study question. No power calculations were presented, but the sample size appears to have been sufficient to detect important differences when compared with other studies from the same medical area. One important concern in the analysis was the

differences in baseline characteristics between the groups in terms of some items. It was unclear whether adjustments were made to correct for potential bias, which might have had an important impact on the final clinical conclusion and on the internal validity of the study.

## Validity of estimate of measure of benefit

As clinical effectiveness was shown to have similar outcomes between the groups, the analysis was considered to be a cost-minimisation study. The reader is therefore referred to the comments in the 'Validity of estimate of measure of effectiveness' field (above).

## Validity of estimate of costs

The perspective adopted was that of the UK NHS. As such, it appears that the relevant cost categories have been included. No detailed resource use information was presented, which makes it difficult to identify what items were included in each category. The unit costs were taken from valid national sources. However, the assumption of using the acquisition costs of valdecoxib instead of the real price might have influenced the final results. This parameter should have been explored in the sensitivity analysis. In addition, it was not specified in the paper how the costs of serious adverse events were estimated in both groups. Finally, this analysis was carried out using data from 26 countries, and no attempt appears to have been made to identify whether pooling the data was representative to the UK. It is widely accepted that different countries incur different opportunity costs. Hence, pooling resource use data from different countries requires special consideration. The internal validity of this analysis was not clear.

## Other issues

The authors compared their results with similar economic evaluations in the same field and made appropriate recommendations. It was not clear whether the results of the study could be generalised as, although data from different countries were pooled, inappropriate methods were used. The authors acknowledged this limitation in their conclusions. The results of the study were not presented selectively. The authors also recognised that using the correct unit cost for valdecoxib might have impacted on the overall results.

## Implications of the study

The results of the study, combined with further evidence from economic studies of celecoxib and rofecoxib, support the rationale for the development of COX-2 specific inhibitors and suggest that their use can reduce the burden of NSAID-associated upper gastrointestinal adverse events.

## Source of funding

## Bibliographic details

von Scheele B, Pena B, Wong J, Niculescu L. Economic evaluation of oral valdecoxib versus diclofenac in the treatment of patients with rheumatoid arthritis in a randomized clinical trial. Rheumatology 2003; 42(Supplement 3): 53-59

## Other publications of related interest

Pettitt D, Goldstein JL, McGuire A et al. Overview of the Arthritis Cost Consequence Evaluation System (ACCES): a flexible pharmacoeconomic model for celecoxib. Rheumatology 2000;39 Suppl 2:33-42.

Haglund U, Svarvar P. The Swedish ACCES model: predicting the health economic impact of celecoxib in patients with osteoarthritis or rheumatoid arthritis. Rheumatology 2000;39 Suppl 2:51-6.

Svarvar P, Aly A. Use of the ACCES model to predict the health economic impact of celecoxib in patients with osteoarthritis or rheumatoid arthritis in Norway. Rheumatology 2000;39 Suppl 2:43-50.

Pavelka K, Recker DP, Verburg KM. Valdecoxib is as effective as diclofenac in the management of rheumatoid arthritis with a lower incidence of gastroduodenal ulcers: result of a 26-week trial. Rheumatology 2003;42:1207-15.

**Indexing Status**

Subject indexing assigned by NLM

**MeSH**

Administration, Oral; Adult; Aged; Aged, 80 and over; Arthritis, Rheumatoid /drug therapy /economics; Cohort Studies; Comparative Study; Cost Savings; Cost-Benefit Analysis; Diclofenac /administration & dosage /economics; Drug Costs; Female; Health Resources /utilization; Hospitalization /economics /statistics & numerical data; Humans; Isoxazoles /administration & dosage /economics; Male; Middle Aged; Peptic Ulcer /chemically induced /economics /prevention & control; Research Support, Non-U.S. Gov't; Sulfonamides /administration & dosage /economics

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