

THE TOTAL COST OF TREATMENT AND THE COST-EFFECTIVENESS OF VALDECOXIB vs DICLOFENAC IN THE TREATMENT OF PATIENTS WITH OSTEOARTHRITIS (OA) OF THE HIP AND/OR KNEE

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INTRODUCTION

- Cyclooxygenase-2 (COX-2) specific inhibitors have similar efficacy profiles to non-specific nonsteroidal anti-inflammatory drugs (NSAIDs) for the treatment of the signs and symptoms associated with osteoarthritis (OA) and adult-onset rheumatoid arthritis (RA). However, COX-2 specific inhibitors are associated with a decreased risk of gastrointestinal (GI) adverse events compared with non-specific NSAIDs.^{1,3}
- Pharmacoeconomic studies of COX-2 specific inhibitors have demonstrated economic advantages compared with other treatments for OA and RA because of their favorable GI safety profile.^{4,6}
- The COX-2 specific inhibitor valdecoxib is approved in Europe for the relief of the signs and symptoms of OA and adult RA (10 and 20 mg qd) and for the treatment of primary dysmenorrhea (40 mg qd).
- Healthcare resource utilization data were prospectively collected in this trial for the purpose of performing economic evaluations comparing valdecoxib and diclofenac.

OBJECTIVE

- To compare the cost-effectiveness and the total cost differences between valdecoxib 10 or 20 mg qd and diclofenac slow release (SR) 75 mg bid in the treatment of OA of the knee and/or hip based on prospectively collected healthcare resource utilization data from a randomized controlled trial (RCT) over 12 months. The perspective of the UK National Health Service (NHS) was used.

METHODS

- In a 52-week, double-blind RCT of adult patients with OA of the knee and/or hip, valdecoxib 10 mg qd (n = 259) and 20 mg qd (n = 261) and diclofenac SR 75 mg bid (n = 262) provided noninferior relief of arthritis pain and inflammation, but valdecoxib had a superior safety profile vs diclofenac (Figures 1 and 2, Table 1).⁷

Figure 1. Study design.

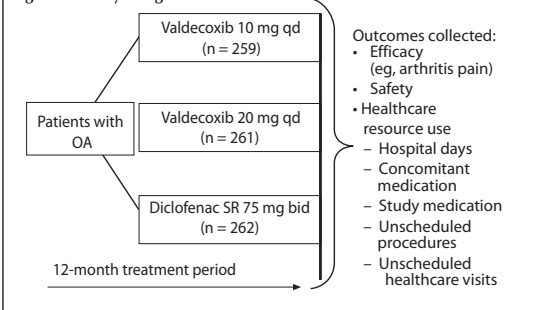


Figure 2. GI safety outcomes for valdecoxib 10 mg qd.

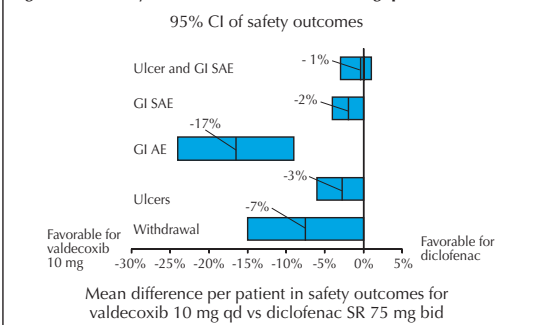


Table 1. Mean Difference per Patient in Efficacy Outcomes* for Valdecoxib 10 mg qd vs Diclofenac SR 75 mg bid

Efficacy Outcome	Mean Difference
Physician's global assessment of arthritis [†]	0.14
WOMAC OA index physical score [‡]	2.38
WOMAC OA index composite score [‡]	3.53
Patient's global assessment of arthritis [†]	0.14
Patient's assessment of arthritis pain [§]	3.48

WOMAC, Western Ontario and McMaster Universities OA index. * Change from baseline at 26 weeks; [†] Scaled 1-5, 1 = very good to 5 = very poor; [‡] Scaled 0-68, 0 = best score to 68 = worst score; [§] Scaled 0-100, 0 = no pain to 100 = most severe pain.

- Healthcare resource utilization data, including hospitalizations, unscheduled healthcare visits, concomitant medications, and unscheduled diagnostic and medical procedures were prospectively collected during the trial.
- This economic evaluation was conducted from a UK NHS perspective, using published UK sources for cost. The most frequent unit costs used in the analysis are found in Table 2.

Table 2. Unit Costs for Resource Utilization Variables (£)

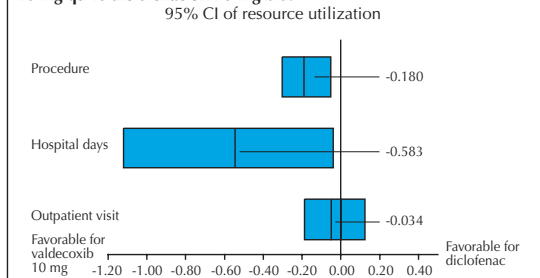
Resource Utilization Variables	Unit Cost, £1 (Range)	Source
Medications		
Valdecoxib 10 and 20 mg qd	£0.77	British National Formulary, 2003
Diclofenac generic 150 mg bid	£0.14	British National Formulary, 2003
Concurrent medications	Variable	Monthly Index of Medical Specialties
Unscheduled outpatient consultations		
General practitioner office visit	£26.00	Personal Social Services Research Unit (PSSRU), 2003
Hospital		
General medicine per day	£151 (£116-£181)	NHS Reference Costs, 2002
GI medical procedures (diagnostic and laboratory)		
Upper GI endoscopy	£178 (£106-£184)	NHS Medical Gastroenterology Reference Costs, 2002

- Total costs per patient were compared between the valdecoxib 10 and 20 mg qd treatment groups and the diclofenac SR 75 mg bid treatment group over the 12-month treatment period.
- Cost per averted ulcer was used as the primary cost-effectiveness measure.
- Incremental cost-effectiveness ratios for the additional cost per successfully treated patient were analyzed for:
 - Avoided symptomatic ulcers (adverse event reported as gastric or duodenal ulcer)
 - Avoided GI adverse event reported as a GI disorder
 - Avoided GI serious adverse event
 - Avoided symptomatic ulcers reported as GI serious adverse event
 - Avoided withdrawal due to treatment failure and/or adverse event.
- The total costs per patient associated with GI serious adverse events over the 12-month period were compared between the valdecoxib 10 and 20 mg qd treatment groups and the diclofenac SR 75 mg bid treatment group to explore whether the difference in GI serious adverse events among the groups had any direct economic implication.
- Bootstrapping was used to create a 95% confidence interval (CI).

RESULTS

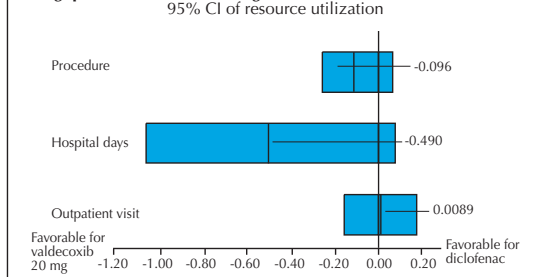
- The treatment groups were comparable with respect to age, race/ethnicity, and gender.
- Valdecoxib 10 and 20 mg qd had clinically noninferior efficacy to diclofenac SR 75 mg bid at all timepoints; none of the 95% CIs overlapped 15 mm on the patient's assessment of arthritis pain (visual analog scale), the smallest difference determined to be clinically meaningful. The mean difference per patient in efficacy outcomes for valdecoxib 10 mg qd compared with diclofenac SR 75 mg bid is shown in Table 1.
- The overall incidence of adverse events was significantly lower in both valdecoxib treatment groups than in the diclofenac treatment group. Significantly fewer patients in the valdecoxib 10 and 20 mg qd treatment groups reported GI adverse events, including abdominal pain and gastric ulcer, than in the diclofenac SR 75 mg bid treatment group (Figure 2).
- Both valdecoxib treatment groups demonstrated a lower mean number of hospital days (valdecoxib 10 mg qd, 0.44 days; valdecoxib 20 mg qd, 0.53 days; diclofenac SR 75 mg bid, 1.02 days) and a smaller percentage of valdecoxib-treated patients were hospitalized (valdecoxib 10 mg qd, 7.3%; valdecoxib 20 mg qd, 8.4%; diclofenac SR 75 mg bid, 9.5%).
- The mean differences in hospital days and procedures were significantly lower for the valdecoxib 10 mg qd treatment group compared with the diclofenac treatment group (Figure 3).

Figure 3. Mean difference in resource utilization counts for valdecoxib 10 mg qd vs diclofenac SR 75 mg bid.



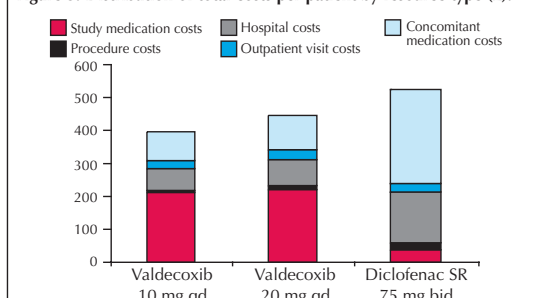
- The differences in hospital days and procedures were also lower for the valdecoxib 20 mg qd treatment group compared with the diclofenac treatment group; however, the differences were not significantly different (Figure 4).

Figure 4. Mean difference in resource utilization counts for valdecoxib 20 mg qd vs diclofenac SR 75 mg bid.



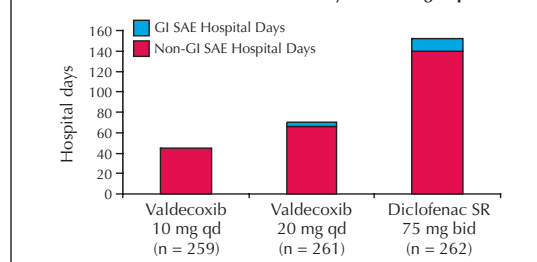
- The differences in resource utilization were reflected in fewer costs for hospitalization and outpatient visits. When study medication costs were included, treatment with valdecoxib 10 mg qd resulted in lower mean total costs than treatment with diclofenac (£395.86 vs £525.07), with a treatment cost difference of -£129.20 (95% CI, -£448.80 to £190.39) per patient over a 12-month period in favor of valdecoxib.
- Treatment with valdecoxib 20 mg qd also resulted in lower mean total costs than treatment with diclofenac (£445.33 vs £525.07), with a treatment cost difference of -£79.74 (95% CI, -£400.92 to £241.44).
- Study medication costs comprised the largest part of the resource uses in the valdecoxib treatment groups followed by concomitant medication costs.
- In the diclofenac treatment group, concomitant medication costs comprised the largest portion of total costs with hospitalization costs being the second largest cost component. The distribution of total costs per patient by resource type are shown in Figure 5.

Figure 5. Distribution of total costs per patient by resource type (£).



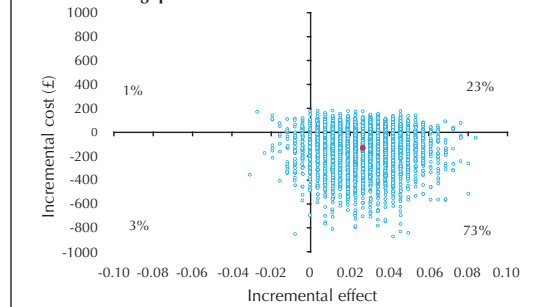
- Patients in the valdecoxib 10 mg qd treatment group had fewer GI serious adverse event-related hospitalization days, and both valdecoxib treatment groups had fewer non-GI serious adverse event-related hospitalization days compared with the diclofenac treatment group.
- The mean number of hospital days (including GI and non-GI serious adverse event-related hospitalization days) was significantly lower for the valdecoxib 10 mg qd treatment group compared with the diclofenac SR 75 mg bid treatment group (0.58 more hospitalization days per patient in the diclofenac treatment group; 95% CI, -1.12 to -0.05). Additionally, the mean number of hospitalization days (including GI and GI serious adverse event-related days) was lower in the valdecoxib 20 mg qd treatment group compared with the diclofenac SR 75 mg bid treatment group (0.49 more hospitalization days per patient in the diclofenac treatment group; 95% CI, -1.06 to 0.07) (Figure 6).

Figure 6. Comparison of hospitalization days due to GI serious adverse events and non-GI serious adverse events by treatment group.



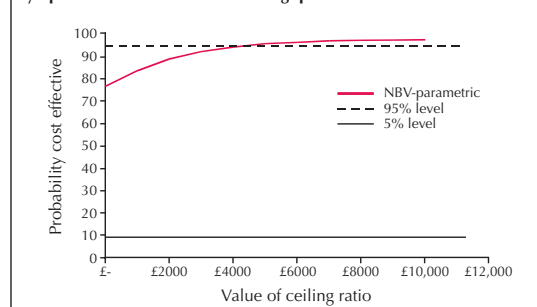
- The cost-effectiveness plane shows the probability that valdecoxib 10 mg qd is cost saving for avoiding an additional occurrence of symptomatic ulcer. A high percentage of the valdecoxib samples are found in the first (23%) and second (73%) quadrants, indicating that valdecoxib is more effective in most cases and costs less than diclofenac in 73% of the cases (Figure 7).

Figure 7. Cost-effectiveness plane for avoided symptomatic ulcer valdecoxib 10 mg qd.



- The cost-effectiveness acceptability curve for valdecoxib 10 mg qd is presented in Figure 8.

Figure 8. Cost-effectiveness acceptability curve for avoided symptomatic ulcer valdecoxib 10 mg qd.



- The cost-effectiveness plane and acceptability curve for valdecoxib 20 mg qd were similar to those for valdecoxib 10 mg qd (Data not shown).
- At either dose, cost per averted ulcer showed valdecoxib as the dominant therapy with fewer ulcers and lower total medical costs.

CONCLUSIONS

- The improved safety profile of valdecoxib 10 and 20 mg qd results in lower costs for healthcare resource utilization compared with diclofenac SR 75 mg bid.
- Most of this decrease in cost is attributable to fewer hospital days as a result of fewer serious adverse events in the valdecoxib treatment groups.
- The use of valdecoxib in daily doses of 10 and 20 mg for the treatment of adult patients with OA resulted in significantly fewer symptomatic ulcers ($P < 0.05$) at a lower average cost per patient over a 12-month period compared with diclofenac (nonsignificant).
- As measured by the cost per averted ulcer, valdecoxib seems to be a cost-effective treatment compared with diclofenac in the population represented in this trial.

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