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## Comparison of the incidence rates of gastrointestinal and thromboembolic events reported for patients prescribed celecoxib and meloxicam in general practice in England using PEM data

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### Focal points

- The NICE report indicated that there is limited good quality, comparative data available on COX-2 selective inhibitors
- We have monitored the safety of celecoxib and meloxicam during their immediate post-marketing period in England, using the non-interventional observational cohort technique of prescription-event monitoring
- We report a relatively lower rate of symptomatic (acid/peptic) GI events and complicated upper GI conditions (perforations/bleeding) in users of celecoxib compared with meloxicam
- We also report a differential channelling effect of patients at higher risk of GI problems onto celecoxib

### Introduction

In the United Kingdom in July 2001, the National Institute for Clinical Excellence (NICE) issued guidance on the use of cyclo-oxygenase (COX)-2 selective inhibitors for treatment of osteoarthritis and rheumatoid arthritis.<sup>1</sup> However, the report indicated that there is limited good quality, comparative data available between these agents, especially with regard to gastrointestinal (GI) or cardiovascular (CV) adverse events.<sup>2</sup> The Southampton drug safety research unit monitored the safety of rofecoxib, celecoxib and meloxicam during the post-marketing period in England, using the non-interventional observational cohort technique of prescription-event monitoring (PEM).<sup>3</sup> In view of professional and regulatory interest, we undertook a series of studies, using PEM data for each of these drugs, to examine and compare their GI and CV thromboembolic (TE) adverse event profiles.<sup>4,5</sup> The aims of this second set of studies were to investigate whether there were differences in the incidence of reported GI events associated with symptomatic ulcers (acid/peptic symptoms), serious complicated ulcers (perforations and GI bleeds), or selected TE (cardiovascular, cerebrovascular or peripheral venous thrombotic) events in two large cohorts of patients prescribed either celecoxib or meloxicam by general practitioners (GPs) under primary care conditions.

### Method

The retrospective studies were conducted using PEM data. Exposure data was derived from dispensed prescriptions written by GPs for celecoxib (May 2000 to November 2001) and meloxicam (December 1996 to March 1997). Demographic and outcome data (clinical events), plus information on selected risk factors (Table 1) were collected from questionnaires posted to prescribers at least six months after the date of the first dispensed prescription for each patient. Incidence rates of the first event within each GI and TE group for the 270-day period after starting treatment, and crude and adjusted rate ratios (RR) were calculated using Poisson regression modelling.

### Results

Patients prescribed celecoxib were more likely than those prescribed meloxicam to have an indication of osteoarthritis (28.1 vs 23.2 per cent), be female (68.3 vs 67.1 per cent), be aged 65 years or more (47.5 vs 43.1 per cent), have been prescribed NSAIDs within three months of starting treatment (49.4 vs 47.9 per cent) and have a past history of upper GI conditions (54.7 vs 29.2 per cent), all  $\chi^2$ ,  $P < 0.02$ .

### Discussion

The GI study reports a relatively lower rate of symptomatic (acid/peptic) GI events and complicated upper GI conditions (perforations/bleeding) in users of celecoxib compared with meloxicam. Furthermore, a differential chan-

**Table 1** Crude and adjusted rate ratios of selected GI and TE events in users of celecoxib compared with meloxicam

Event	Number of events (%) [Rate per 1,000 person-years (95 per cent CI)]		Adjusted rate ratio(95 per cent CI) and number of observations included in the model (n)
	Celecoxib (n=17,458)	Meloxicam (n=19,087)	
Symptomatic (acid/peptic) upper GI	1054 (6.04) [186.37 (175.45,197.97)]	1376 (7.21) [188.80 (179.08,199.04)]	0.77 (0.69,0.85) * n=22211
Complicated upper GI conditions (perforations/bleeding)	42 (0.24) [7.29 (5.39,9.86)]	67 (0.35) [8.93 (7.03,11.34)]	0.56 (0.32,0.96) * n=22195
Cardiovascular TE	28 (0.16) [4.73 (3.26,6.85)]	19 (0.10) [2.53(1.61,3.97)]	1.72 (0.87,3.40) † n=27329
Cerebrovascular TE	68 (0.39) [11.51 (9.07,14.59)]	52 (0.27) [0.69 (0.52,0.90)]	1.66 (1.10,2.51) † n=27329
Peripheral venous TE	17 (0.10) [2.87 (1.79,4.62)]	20 (0.10) [2.66 (1.72,4.13)]	1.06 (0.51,2.19) † n=27329

\* Adjusted for age, (age<sup>2</sup>), sex, indication, and risk factors (medical history of upper GI problems and whether prescribed NSAIDs within 3 months prior to starting drug);

† Adjusted for age, (age<sup>2</sup>), and sex only.

nelling effect of patients at higher risk of GI problems onto celecoxib was observed. In the TE study, the incidence of each group of TE events for both drug cohorts was less than 0.5 per cent; however a relatively higher rate of cerebrovascular TE events was observed in users of celecoxib compared with meloxicam with no difference in the rate of cardiovascular TE, or peripheral venous thrombotic events between these two drug cohorts. The results of these studies should be considered together with results of other clinical and pharmacoepidemiological studies on this topic.

### References

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