Safety and Efficacy of Meloxicam in the Treatment of Osteoarthritis

A 12-Week, Double-blind, Multiple-Dose, Placebo-Controlled Trial

David Yocum, MD; Roy Fleischmann, MD; Paul Dalgin, MD†; Jacques Caldwell, MD; David Hall, PhD; Paul Roszko, RPh; for the Meloxicam Osteoarthritis Investigators

Background: Meloxicam (Mobic; Boehringer Ingelheim, Ridgefield, Conn) is an enolic acid derivative of the oxicam group of nonsteroidal anti-inflammatory drugs (NSAIDs) whose mechanism of action may be related to prostaglandin (cyclooxygenase) synthetase inhibition. In previous studies, meloxicam has been found to be safe and effective in the treatment of osteoarthritis (OA) at doses of 7.5 to 15 mg daily. To evaluate a lower dose and a different patient population, we evaluated the efficacy and safety of 3 doses of meloxicam vs placebo and diclofenac for the treatment of OA among patients with symptom exacerbations.

Methods: In this double-blind, double-dummy, parallel-group, multicenter study, 774 patients with confirmed OA of the hip or knee and a flare were randomized and treated with daily oral administration of meloxicam tablets (at dosages of 3.75, 7.5, or 15 mg/d), diclofenac (100 mg [50 mg twice daily]), or placebo. Treatment was for 12 weeks, with regular assessments for drug safety and efficacy. Safety was assessed by evaluation of adverse events, vital signs, and laboratory data. Primary efficacy variables included the Western Ontario and McMaster University Osteoarthritis (WOMAC) index, the patient’s overall assessment of pain, and the investigator’s overall assessment of disease activity.

Results: The incidence of all adverse events was lower at each dosage of meloxicam than for diclofenac but greater than for placebo. However, the incidence of gastrointestinal adverse events and dropout rates because of such events was the same for meloxicam as for placebo and lower than for diclofenac. Meloxicam, at 7.5 and 15 mg/d, and diclofenac were statistically significantly more effective than placebo for all end points, while the 3.75-mg/d dosage of meloxicam did not always reach statistical significance for all end points. Efficacy was evident after 2 weeks of treatment, improved with increasing doses, and was maintained until the end of the trial.

Conclusions: Meloxicam is a safe and effective medication for the symptomatic treatment of OA. The data support consideration of 7.5 to 15 mg of meloxicam once daily to treat the pain and stiffness of OA, with gastrointestinal tolerability comparable to that of placebo.

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OSTEOARTHRITIS (OA) is a chronic degenerative joint disease that, although radiologically detectable in a broad population, typically becomes symptomatic in the elderly. The prevalence of OA increases with age, resulting not only in substantial medical costs. Use of NSAIDs has been associated with a risk of serious and life-threatening gastrointestinal (GI) adverse events, such as perforation and bleeding. Although these events are of great concern, they are uncommon. One study estimated the annual rate of hospitalizations for upper GI adverse events in OA patients taking NSAIDs to be 0.4%. Much more common are adverse effects such as dyspepsia, nausea, and vomiting. While these adverse effects do not correlate with GI bleeding, they do impact the performance of daily functions and contribute to increased medical costs resulting from the need for additional physician visits and changes in medication.

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From the Arizona Arthritis Center, University of Arizona, Tucson (Dr Yocum); Rheumatology Associates, Dallas, Tex (Dr Fleischmann); Arthritis and Allergy Institute, Daytona Beach, Fla (Dr Caldwell); and Boehringer Ingelheim, Ridgefield, Conn (Dr Hall and Mr Roszko).

A list of the Meloxicam Osteoarthritis Investigators is given on page 2954.

†Deceased. Dr Dalgin was in a private practice in Stamford, Conn.
Meloxicam is an enolic acid derivative of the oxicam group of NSAIDs. It has been approved for use in more than 80 countries for the treatment of OA, rheumatoid arthritis, and ankylosing spondylitis. In vitro and in vivo tests have shown that meloxicam is a cyclooxygenase (COX) inhibitor that demonstrates more COX-2 inhibition than COX-1 inhibition at therapeutic concentrations. Its pharmacokinetic profile suggests good bioavailability with once-daily dosing. The drug is readily absorbed and widely distributed with no accumulation in any tissue. Steady-state plasma concentrations are reached after 3 to 5 days with administration of 7.5 and 15 mg/d, with a plasma elimination half-life of 20 hours. Meloxicam is extensively protein bound (99%) and is metabolized in the liver, with equal excretion of inactive metabolites in the urine and feces. In 6-month, double-blind trials, meloxicam, 15 mg/d, is comparable to piroxicam, 20 mg/d, and diclofenac, 100 mg/d.

The objective of the present study was to evaluate the safety and efficacy of 3 dosages of meloxicam (3.75, 7.5, and 15 mg/d) in comparison with placebo and an active comparator, diclofenac, in patients whose disease flared when their previous NSAID was withdrawn.

Among a total of 1091 patients enrolled and screened by 61 study centers, 779 patients were randomized into the trial, and 774 patients initiated treatment. The demographic and disease characteristics were similar across the treatment groups (Table 1). The ratio of women to men was 2:1, and the mean ± SD age of the patient population was 62.9 ± 10.3 years; approximately 25% of the patients were at least 70 years of age. Duration of OA was greater than 5 years in more than 50% of the patients. Osteoarthritis of the knee was more prevalent as the target joint (82% of patients) than OA of the hip. Almost 90% of patients had OA in more than 1 joint. The mean total duration of prior NSAID use ranged from 3.8 to 4.1 years.

Among the randomized groups, 5 patients took no trial medication and 5 patients were lost to follow-up before any post-baseline efficacy evaluations could be per-

The WOMAC index is based on Likert scales that allow the patient to self-evaluate the status of his or her condition. The assessment consists of 3 subscales (for pain, stiffness, and physical function), as well as a total score (ranging from 0 [best] to 100 [worst]). In addition to the WOMAC subscale for pain, the patient’s overall pain for the prior 24 hours was assessed using a 100-mm VAS (0, no pain; 100, worst pain).

A 100-mm VAS was also used in the patient’s global assessments of disease activity, with the best outcome fixed at 0 and the worst outcome fixed at 100. The investigator’s global assessment of disease activity used a 5-point verbal rating scale (range from 0 to 4: none, mild, moderate, severe, and very severe) and was performed after and blinded to the patient’s global assessment.

Secondary efficacy variables included assessment of pain both at rest and on movement for the previous 24 hours in the target joint. As in the primary efficacy end point for pain, a 100-mm VAS was used. Use of rescue medication (acetaminophen) was permitted, and the rate of consumption on treatment was included as a secondary efficacy variable. At 12 weeks or with early termination, a final global assessment of efficacy was performed by the patient and the investigator using a 4-point verbal rating scale (good, satisfactory, not satisfactory, and poor). In addition, the patient’s status with regard to the change in arthritic condition was determined by asking the patient to rate his or her current condition compared with the condition at the start of the trial as improved, unchanged, or deteriorated.

STATISTICAL METHODS
To establish the superiority of meloxicam over placebo, a type I error was maintained by comparing meloxicam, 15 mg/d, with placebo, and subsequently comparing meloxicam, 7.5 and 3.75 mg/d, with placebo if, and only if, the next highest dose was significantly better than placebo (P ≤ .05). It was determined that, to demonstrate efficacy differences between placebo and meloxicam at a significance level of P ≤ .05 with an overall power of 80%, a sample size of 700 patients (140 per treatment arm) would be required.

Safety and tolerability data were analyzed using χ² analysis or the Fisher exact test on data regarding the rates of adverse events and the rates of patient withdrawals (overall and due to adverse events). Time to first GI adverse event was analyzed with log-rank tests and Kaplan-Meier estimates.

Primary efficacy analyses were performed based on the intent-to-treat principle, including all treated patients with at least one on-treatment evaluation. Both the patient’s last visit assessment (last observation carried forward) and the weighted mean of all on-treatment assessments were analyzed. Analysis of variance models, including treatment, target joint, and center, were used for all variables assessed by VAS, as well as for the WOMAC index (for pain, stiffness, physical function, and total score). These variables were analyzed as change from baseline (intensity of flares). Pairwise differences between the adjusted means for treatments were calculated along with P values and 2-sided 95% confidence intervals for these differences.

Secondary efficacy variables were also analyzed applying the intent-to-treat principle. For those variables assessed by VAS (pain on movement and pain at rest), analyses were performed using analysis of variance on data for change from baseline in a manner similar to that for the primary analyses. For rescue medication use, analysis of covariance was performed, with weekly average use as the dependent variable and use during flare as a covariate. The patients’ and investigators’ final global assessment of efficacy and the patients’ assessment of change in arthritic condition were analyzed using stratified rank sum test procedures, stratified by center. Time to early discontinuation (overall, for adverse events, and for lack of efficacy) was analyzed with log-rank tests and Kaplan-Meier estimates. Time to first GI adverse event was analyzed with adjustment for exposure by applying log-rank tests and the Kaplan-Meier algorithm.


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formed; they are therefore excluded from the efficacy evaluation (n = 769). However, all patients who were randomized and received at least 1 dose of trial medication are included in the safety evaluation (n = 774).

SAFETY AND TOLERABILITY
The incidence of all adverse events was comparable among the 3 meloxicam groups (58.4%, 55.8% and 57.7% for 3.75, 7.5, and 15 mg/d, respectively) and was higher than in the placebo group (47.8%) and lower than in the diclofenac group (66.0%). Meloxicam did not demonstrate any dose-dependent increase in total adverse events or adverse events grouped by preferred terms (Table 2) based on the World Health Organization Adverse Event coding thesaurus (World Health Organization Adverse Event Dictionary, September 1995).

Gastrointestinal adverse events were the most frequently reported events by system organ class (Table 2). There were no significant differences in the incidence of GI adverse events between the placebo and meloxicam groups, including the pooled meloxicam group, which differed from the placebo group by less than 2% (χ², P > .70). There were significantly more patients with GI adverse events in the diclofenac group than in the placebo group (χ², P < .02). After Kaplan-Meier adjustments for dropout rates, estimated 12-week GI adverse event rates were 18% for meloxicam, 15 mg/d; 21% for placebo and meloxicam, 3.75 and 7.5 mg/d; and 30% for diclofenac (Figure 1). Log-rank tests indicated that meloxicam was significantly different from diclofenac (P < .02) but not from placebo (P > .95). Other adverse effects, such as headache, rash, and edema, were not significantly different between any of the meloxicam, placebo, and diclofenac groups (P > .05 for all events; data not shown).

Withdrawals due to adverse events over the 12-week period were similar among the meloxicam and diclofenac groups (7% to 9%) and were not significantly different than for the placebo group (3.8%) (P > .50) (Table 3). Kaplan-Meier estimates of withdrawal due to adverse events are 8% to 10% for the active drugs and 7% for placebo (Table 4). Likewise, the percentage of
withdrawals as a result of GI adverse events was similar among the meloxicam groups (3.2%, 3.2%, and 3.8%, respectively, for 3.75, 7.5, and 15 mg/d) and the diclofenac group (4.6%) and not significantly different from the placebo group (1.3%).

The incidence of serious adverse events was similar among the meloxicam and diclofenac groups (3.3%) and was slightly higher than for patients receiving placebo (1.3%; P > .05). A serious adverse event was defined as any fatal or immediately life-threatening clinical experience or disabling event, or one that required prolonged inpatient hospitalization, whether or not it was judged to be related to treatment. Only 1 GI event was considered to be a serious adverse event and also thought to be related to study medication. A patient receiving meloxicam, 15 mg/d, with a history of intermittent diverticulitis experienced GI bleeding 17 days after beginning therapy that was believed to be because of active diverticulosis as diagnosed by colonoscopy. There was 1 death in this trial, in the 3.75-mg/d meloxicam group, that was a result of coronary insuffi-

### Table 1. Demographic and Baseline Disease Characteristics for All Treated Patients*

<table>
<thead>
<tr>
<th>Sex</th>
<th>Placebo (n = 157)</th>
<th>Meloxicam, 3.75 mg/d (n = 154)</th>
<th>Meloxicam, 7.5 mg/d (n = 154)</th>
<th>Meloxicam, 15 mg/d (n = 156)</th>
<th>Diclofenac, 50 mg BID (n = 153)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>55 (35.0)</td>
<td>51 (33.1)</td>
<td>57 (37.0)</td>
<td>56 (35.9)</td>
<td>49 (32.0)</td>
</tr>
<tr>
<td>Female</td>
<td>102 (65.0)</td>
<td>103 (66.9)</td>
<td>97 (63.0)</td>
<td>100 (64.1)</td>
<td>104 (68.0)</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>143 (91.1)</td>
<td>139 (90.3)</td>
<td>141 (91.6)</td>
<td>140 (89.7)</td>
<td>136 (88.9)</td>
</tr>
<tr>
<td>African American</td>
<td>10 (6.4)</td>
<td>9 (5.8)</td>
<td>8 (5.2)</td>
<td>7 (4.5)</td>
<td>13 (8.5)</td>
</tr>
<tr>
<td>Other</td>
<td>4 (2.5)</td>
<td>6 (3.9)</td>
<td>5 (3.2)</td>
<td>9 (5.8)</td>
<td>4 (2.6)</td>
</tr>
<tr>
<td>Age, y</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 60</td>
<td>68 (43.3)</td>
<td>63 (40.9)</td>
<td>68 (44.2)</td>
<td>57 (36.5)</td>
<td>66 (41.3)</td>
</tr>
<tr>
<td>&gt; 60</td>
<td>50 (31.8)</td>
<td>55 (35.7)</td>
<td>49 (31.6)</td>
<td>58 (37.2)</td>
<td>45 (28.4)</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>62.3 ± 10.8</td>
<td>62.3 ± 10.5</td>
<td>62.4 ± 10.2</td>
<td>64.3 ± 9.9</td>
<td>63.0 ± 10.0</td>
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<tr>
<td>Target joint</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hip</td>
<td>25 (15.9)</td>
<td>24 (15.6)</td>
<td>31 (20.1)</td>
<td>25 (16.0)</td>
<td>34 (22.2)</td>
</tr>
<tr>
<td>Knee</td>
<td>132 (84.1)</td>
<td>130 (84.4)</td>
<td>123 (79.9)</td>
<td>131 (84.0)</td>
<td>119 (77.8)</td>
</tr>
<tr>
<td>Osteoarthritis other than target joint</td>
<td>139 (88.5)</td>
<td>141 (91.6)</td>
<td>140 (90.9)</td>
<td>138 (88.5)</td>
<td>136 (88.9)</td>
</tr>
<tr>
<td>Duration of osteoarthritis, y</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 5</td>
<td>73 (46.5)</td>
<td>73 (47.4)</td>
<td>73 (47.4)</td>
<td>89 (57.1)</td>
<td>74 (48.4)</td>
</tr>
<tr>
<td>&gt; 5</td>
<td>84 (53.5)</td>
<td>81 (52.6)</td>
<td>81 (52.6)</td>
<td>67 (42.9)</td>
<td>79 (51.6)</td>
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<tr>
<td>Mean ± SD</td>
<td>8 ± 7.2</td>
<td>9 ± 9.4</td>
<td>8 ± 8.4</td>
<td>7 ± 8.8</td>
<td>9 ± 8.3</td>
</tr>
<tr>
<td>History of peptic ulcer bleeding</td>
<td>11 (7.0)</td>
<td>16 (10.4)</td>
<td>11 (7.1)</td>
<td>8 (5.1)</td>
<td>16 (10.5)</td>
</tr>
<tr>
<td>Duration of prior NSAID use, mean ± SD, y</td>
<td>4.0 ± 4.4</td>
<td>4.1 ± 5.0</td>
<td>3.8 ± 4.3</td>
<td>3.8 ± 4.4</td>
<td>3.9 ± 4.8</td>
</tr>
</tbody>
</table>

* BID indicates twice daily; NSAID, nonsteroidal anti-inflammatory drug.

### Table 2. Adverse Events*

<table>
<thead>
<tr>
<th>Any adverse event†</th>
<th>Placebo (n = 157)</th>
<th>Meloxicam, 3.75 mg/d (n = 154)</th>
<th>Meloxicam, 7.5 mg/d (n = 154)</th>
<th>Meloxicam, 15 mg/d (n = 156)</th>
<th>Diclofenac, 50 mg BID (n = 153)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any GI adverse event‡</td>
<td>27 (17.2)</td>
<td>30 (19.5)</td>
<td>31 (20.1)</td>
<td>27 (17.3)</td>
<td>88 (19.0)</td>
</tr>
</tbody>
</table>

* BID indicates twice per day; GI, gastrointestinal.
† Excluding GI adverse events, but including all other adverse events that occurred at an incidence of 5% or greater.
‡ All GI adverse events that occurred at an incidence of 2% or greater.
ciency and was deemed by the treating physician not to be related to treatment. There were no reported occurrences of upper GI tract perforations, ulcerations, or peptic ulcer bleedings in any of the treatment groups.

There were no statistically significant changes in mean laboratory values in any of the active treatment groups compared with placebo. There was a slight increase in alanine aminotransferase and aspartate aminotransferase mean values with diclofenac that was not observed in the meloxicam treatment groups or the placebo group.

**EFFICACY**

Baseline values (flare) were similar across all treatment groups for each efficacy end point and demonstrated worsening from the values recorded at screening during prior NSAID use. At the end of treatment, all treatment groups had improved from their flare disease state, demonstrating significant improvement ($P<.001$) from baseline. Efficacy of meloxicam and diclofenac became evident early in treatment (2 weeks) (Figure 2). Efficacy is evident by 28 days in comparing the withdrawals due to lack of efficacy in the placebo group with the withdrawals in the meloxicam and diclofenac treatment groups (Table 4). The difference between the 3.75-mg/d meloxicam dosage and the higher dosages of meloxicam is also clear, with a withdrawal rate of 18% in the 3.75-mg/d group and a 9% withdrawal rate in the 7.5- and 15-mg/d groups. Overall, patients in the meloxicam and diclofenac groups had statistically significantly lower rates of withdrawal for lack of efficacy than the placebo group (41%): 18%, 17%, and 12% for meloxicam, 7.5 and 15 mg/d, and diclofenac, respectively ($P<.001$), and 31% for meloxicam, 3.75 mg/d ($P<.01$). Withdrawal rates due to lack of efficacy were also significantly lower for meloxicam, 7.5 and 15 mg/d, and for diclofenac than for meloxicam, 3.75 mg/d ($P<.01$). Both meloxicam and diclofenac produce symptomatic reductions to below pre-flare levels, while placebo patients are less successful in recovering from NSAID withdrawal (Figure 2).

The WOMAC index consists of a total score and 3 subscales for pain, physical function, and stiffness. At the final visit (Figure 3 and Table 5) and for on-treatment weighted means (data not shown), meloxicam, 7.5 and 15 mg/d, and diclofenac were significantly superior to placebo for all WOMAC efficacy parameters. Meloxicam exhibited dose-dependent efficacy that was most pronounced for the WOMAC pain and stiffness subscales and was reflected in the total WOMAC score (Figure 3). The 3.75-mg/d dosage of meloxicam proved superior to placebo only for the WOMAC stiffness subscale at the final assessment.

Similar results were obtained for the patient’s overall assessment of pain and the patient’s global assess-
ment of disease activity. Meloxicam, 7.5 and 15 mg/d, and diclofenac demonstrated significant improvement over placebo (P < .005) for patient’s overall assessment of pain, and all active treatment groups were statistically significantly better than placebo in the patient’s overall assessment of disease activity (P < .05 for meloxicam, 3.75 mg/d, and P < .001 for diclofenac and meloxicam, 7.5 and 15 mg/d) (Table 5).

At baseline, 60% of patients were rated as having severe or very severe disease activity by the investigator’s assessment of disease activity. At the final visit, the proportion of patients with severe or very severe disease activity in the meloxicam, 7.5- and 15-mg/d, groups (12% and 13%, respectively) and in the diclofenac group (15%) was approximately half that in the placebo group (30%) (P < .01 for all comparisons with placebo).

Results for secondary efficacy variables were consistent with those observed for the primary variables. For pain on movement, both meloxicam at 7.5 mg and 15 mg/d and diclofenac demonstrated significantly better efficacy than placebo (P < .01), and for pain at rest, all 3 meloxicam dosages were significantly better than placebo (P ≤ .001 for meloxicam, 7.5 and 15 mg/d, and diclofenac; and P < .05 for meloxicam, 3.75 mg/d.

For both patient’s and investigator’s final global assessment of efficacy, the 7.5- and 15-mg/d dosages of meloxicam and diclofenac were statistically significantly superior to placebo for all comparisons (data not shown). The mean rate of consumption of rescue medication on treatment was significantly lower (P < .05) in all the meloxicam groups compared with placebo (12.0 tablets per week for placebo and 9.7, 8.5, and 8.4 tablets per week for meloxicam 3.75, 7.5, and 15 mg/d, respectively). When patients were asked to evaluate their change in disease status with respect to the start of the trial, the percentage of patients reporting improvement increased as the dosage of meloxicam increased (29.7%, 37.9%, 47.7%, 55.8%, and 57.9% for placebo; meloxicam, 3.75, 7.5, and 15 mg/d; and diclofenac, respectively).
The greatest percentage of patients reporting unchanged or deteriorated arthritic activity was in the placebo and 3.75-mg/d meloxicam groups. However, the 3.75-mg/d meloxicam group was still statistically significantly superior to placebo for this end point (P < .05), as were the 2 higher dosages of meloxicam (P < .001). A comparison of the end point values with the values at screening (prior to previous NSAID washout) for the efficacy variables shows that the magnitude of patient improvement with meloxicam is at least equal to that of the observed flare. Figure 2 shows the patient’s overall assessment of pain at screening, at baseline (flare), and during the course of treatment until the end of the trial (last observation carried forward). Similar results were obtained for other efficacy variables.

Meloxicam, 7.5 and 15 mg/d, proved to be effective, safe, and well tolerated for the treatment of OA and was statistically superior to placebo and similar to diclofenac for all primary and secondary efficacy parameters. Moreover, the uniform incidence of GI adverse events across the meloxicam dosage groups was similar to that for placebo and lower than that for diclofenac.

Among patients taking NSAIDs, GI adverse events, such as dyspepsia, nausea, and vomiting, can add considerably to the cost of treatment. These adverse effects, though not predictive of more serious GI injury, lead to treatment interruptions and drug switching and add to treatment costs when additional physician visits or concomitant medications are required. In one study, the incidence of dyspepsia was approximately 16% in NSAID users, and it has been suggested that the incidence may be as high as 50% to 60% depending upon other factors.

In this study, patients were generally elderly (approximately 25% of the patients were ≥70 years of age) and on average had used NSAIDs for about 4 years. In addition, 8% of the patient population had a history of peptic ulcer bleedings of the upper GI tract. Therefore, this population is not highly selected and should be fairly representative of the OA population.

The safety and tolerability of meloxicam in this 12-week trial are consistent with the results of 2 European trials that directly compared the safety and tolerability of meloxicam, 7.5 mg/d, with diclofenac, 100 mg/d, and piroxicam, 20 mg/d, in 17979 patients during a 1-month course of treatment, the standard of care for OA in Europe. In those 2 studies, meloxicam demonstrated significantly better tolerability than these NSAIDs. Other comparative European trials have demonstrated both of these meloxicam doses to be effective in comparison with diclofenac and piroxicam for the treatment of OA, in some trials for as long as 6 months.

The lowest dosage of meloxicam, 3.75 mg/d, reached statistical significance vs placebo for pain at rest and for patient’s assessment of disease activity.

The WOMAC index was designed as a self-administered health status instrument and has been validated specifically for assessment of OA. This tool is especially useful since it is very effective at differentiating treatment effects. A meloxicam dose-response relationship was observed for all 4 WOMAC end points and was especially apparent for the pain and stiffness subscales, as pain and stiffness are the 2 symptoms that most affect and limit functionality. There was a corresponding improvement in the patient’s overall assessment of pain; as the meloxicam dosage increased, however, a clear dose response was not observed as in the WOMAC pain subscale.

In conclusion, the data reported herein confirm and extend previous data showing that meloxicam at dosages of 7.5 to 15 mg/d is an effective, safe, and well-tolerated treatment for OA. Meloxicam demonstrated efficacy with no dose response for GI tolerability-related adverse events, thus allowing for flexibility of dosing.

Table 5. Baseline Values and Change From Baseline at Final Assessment for Efficacy Variables

<table>
<thead>
<tr>
<th>Variable</th>
<th>Placebo (n = 155)</th>
<th>Meloxicam, 3.75 mg/d (n = 153)</th>
<th>Meloxicam, 7.5 mg/d (n = 153)</th>
<th>Meloxicam, 15 mg/d (n = 156)</th>
<th>Diclofenac, 50 mg BID (n = 152)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain on movement</td>
<td>75.1 (±7.9)</td>
<td>73.7 (±23.6)</td>
<td>72.7 (±26.7)</td>
<td>71.7 (±28.4)</td>
<td>75.1 (±30.2)</td>
</tr>
<tr>
<td>Pain at rest</td>
<td>64.7 (±15.5)</td>
<td>64.5 (±21.3)</td>
<td>63.8 (±24.7)</td>
<td>63.9 (±25.8)</td>
<td>63.6 (±25.1)</td>
</tr>
</tbody>
</table>

*Last observation carried forward for early withdrawals. BID indicates twice per day; WOMAC, Western Ontario and McMaster University Osteoarthritis index.
†Range, 0 (best) to 96 (worst).
‡P < .05 compared with placebo.
§P < .001 compared with placebo.
¶Range, 0 (none) to 100 (worst) (100-mm visual analog scale).
#P < .005 compared with placebo.
PP < .01 compared with placebo.
REFERENCES


