International Journal of Medical and Pharmaceutical Research

Online ISSN-2958-3683 | Print ISSN-2958-3675
Frequency: Bi-Monthly
Available online on: https://ijmpr.in/

Original Article

Safety and Effectiveness of Polmacoxib in Patients with Osteoarthritis: A Multicenter Retrospective Real-World Study

Dr Nishikant Madkholkar[1], Dr Kushal Sarda[2], Dr Akhilesh Sharma[3]

[1] Medical Advisor, Alkem laboratories, Mumbai.
[2] General Manager, Alkem laboratories, Mumbai.
[3] Chief Medical officer , Alkem laboratories, Mumbai.

Corresponding Author:

Dr Nishikant Madkholkar
Medical Advisor, Alkem laboratories, Mumbai.

Received: 13-01-2026
Accepted: 30-01-2026
Available online: 17-02-2026

ABSTRACT

Background: Osteoarthritis (OA) is a major cause of chronic pain and disability, and although NSAIDs (Non-steroidal anti-inflammatory drugs) remain central to its management, their long-term use is limited by gastrointestinal and cardiovascular risks. Polmacoxib, a novel COX-2 selective NSAID with additional carbonic anhydrase inhibitory activity, offers effective symptom relief with improved safety.
Methods: This multicenter, retrospective observational study analyzed anonymized electronic health record data of 3,088 patients with OA treated with polmacoxib in routine clinical practice. Pain intensity was assessed on a standardized 0–100 scale at baseline and at 3 and/or 6 weeks. Safety was evaluated by documenting treatment-emergent adverse events, and paired statistical analyses were performed.
Results: The mean patient age was 59.0 ± 12.0 years, with common comorbidities including hypertension (49.8%) and diabetes (36.9%). Polmacoxib significantly reduced pain scores from baseline at 3 weeks (mean change −43.7) and 6 weeks (mean change −42.6; $p < 0.05$). Adverse events related to treatment were uncommon and generally mild, comprising nausea (1.39%), vomiting (1.00%), abdominal pain (0.68%), headache (0.55%), and dizziness (0.39%).
Conclusion: In real-world clinical practice, polmacoxib provided significant short-term pain relief with a favorable safety profile in patients with OA, including those with common comorbidities. These findings support its use as an effective and well-tolerated option for OA management.

Keywords: *COX-2 selective NSAID, Carbonic anhydrase inhibition, Pain reduction.*

INTRODUCTION

Osteoarthritis (OA) remains a chronic musculoskeletal disorder affecting millions of people and a leading cause of pain and disability worldwide. Over the past years, the incidence of OA has increased, and its burden is expected to rise in an aging population. In 2020, 595 million people globally were living with OA, which is equivalent to 7·6% of the global population (1). Age, female sex, obesity, and articular trauma are the foremost risk factors of this disease. This disorder usually affects the knee, hips, hands, and spine, inflicting chronic pain, joint stiffness and functional limitation. Present clinical management on symptomatic relief and maintaining mobility, as there are no definitive cures for OA.

Non-steroidal anti-inflammatory drugs (NSAID) have long been the basis of pharmacologic therapy for OA, provided their effectiveness in reducing pain and inflammation and thereby improving patient quality of life (2). However, conventional non-selective NSAIDs causes deleterious side effects, notably gastrointestinal toxicity, cardiovascular risks, and renal impairment, limiting their long-term usage, especially in elderly individuals. To alleviate GI complications, selective cyclooxygenase-2 (COX-2) inhibitors (coxibs) were developed (3). These coxibs selectively target the COX-2 iso-enzyme that is elevated during inflammation while sparing COX-1, which protects the gastric lining, eventually providing anti-inflammatory analgesic benefits with fewer GI side effects (4). There is strong evidence that suggests that COX-2 inhibitors are better tolerated gastro intestinally than non-selective NSAIDs, causing fewer GI side effects (5).

Polmacoxib is a novel COX-2 selective NSAID with promising advantages in osteoarthritis management, offering effective symptom relief with reduced gastrointestinal risk (3). In addition to COX-2 inhibition, its carbonic anhydrase inhibitory activity may help mitigate NSAID-related increases in blood pressure, potentially supporting a more favorable cardiovascular safety profile (6). Polmacoxib was developed by Crystal Genomics Inc. and first approved in 2015 in South Korea for arthritis management(7). More recently, polmacoxib received approval from the Drug Controller General of India (DCGI) in 2023 for the treatment of primary OA of the knee and hip (8). Several clinical trials have demonstrated its effectiveness and safety; for instance, a phase III trial demonstrated polmacoxib 2 mg to have pain relief efficacy non-inferior to celecoxib and superior to placebo over 6 weeks (9). Despite evidence from these trial there remains a need to understand its performance in real-world settings. Real-world evidence is critical to validate and extend clinical trial findings, capturing effectiveness in a broader patient population and identifying any safety signals in general use. While clinical development of polmacoxib has granted beneficial data, gaps exist regarding its long-term safety and its impact on diverse individuals encountered in everyday care.

This study evaluated the real-world safety and effectiveness of polmacoxib in osteoarthritis focusing on pain relief, functional outcomes, and adverse events. The analysis aimed to bridge the gap between clinical trial evidence and routine clinical practice across a broad OA population.

METHODOLOGY

Study Design

This retrospective, multicenter real-world evidence study analyzed anonymized electronic health record data from hospitals, outpatient clinics, and orthopedic centers to evaluate the safety and effectiveness of polmacoxib in routine osteoarthritis care. Eligible patients were identified from medical records, with prescription and laboratory data extracted for analysis. Ethics Committee approval was obtained before starting of the study and informed consent was waived due to the retrospective use of anonymized data.

Study Population

A total of 3088 patients at multiple centers were included in this retrospective real-world evidence study. Patients were eligible for inclusion if they were diagnosed with osteoarthritis and had received polmacoxib for OA management, with complete medical records available, including baseline assessments, treatment details, and follow-up data. Patients with concomitant inflammatory or autoimmune joint diseases, or with known contraindications or prior adverse reactions to polmacoxib, were excluded from the study.

Study flow and conduct

Baseline characteristics and treatment details were collected from the EHR of patients. Baseline variables included demographics (age, sex. Ethnicity), OA disease features (duration of OA and Joints affected), and comorbidities. Polmacoxib treatment details were extracted, including the prescribed dosage, frequency, and duration of therapy and any concomitant medications for OA.

Study Assessments

Safety of polmacoxib was assessed by recording the incidence and severity of adverse events (AEs) associated with polmacoxib therapy. All AEs recorded in the EHR were catalogued and reported in the study. Efficacy was primarily evaluated through changes in patient-reported pain intensity scores over time. Pain scores at baseline and at follow-up visits (3 weeks and 6 weeks) were collected as available and analyzed. Pain intensity was quantified on a 0-100 scale (either a Visual Analog Scale or Numerical Rating Scale) with high scores indicating worse and low scores indicating less pain

Statistical Analysis

The data collected from the database were analyzed for demographics and clinical characteristics. Data were presented as mean ± SD/SE or number (percentage). Changes in primary and secondary endpoints were analyzed using appropriate statistical tests (e.g., paired t-tests, Wilcoxon signed-rank tests). Descriptive statistics were used for different variables at baseline. The p-value of <0.05 was considered statistically significant.

Ethical Considerations

The study protocol was approved by the Institutional Ethics Committee (IEC). The study adhered to the principles outlined in the Declaration of Helsinki and Good Clinical Practice (GCP) guidelines.

RESULTS

Demographic and Baseline Characteristics

A total of 3088 OA patients were included in the study. Among these OA patients on polmacoxib, 2176 (70.5%) were males and 912 (29.5%) were females. The majority of patients belonged to the age group of 59.01±11.99 years (95% CI:58.59-59.43). The mean body weight and height were 70.05±11.69 kg (95% CI:69.64-70.46) and 163.05±12.18 cm

(95%CI:162.62-163.48). The mean body mass Index (BMI) was 26.41± 4.25 kg/m^2 (95%CI: 26.26-26.56). Regarding comorbid conditions, hypertension was present in 1539 patients (49.8%), diabetes in 1138 patients (36.9%), and cardiovascular diseases in 411 patients (13.3%). All the patients received polmacoxib therapy where 2490 patients (80.6%) underwent a 3-week course, and the remaining 598 patients (19.4%) continued therapy for 6 weeks **(Table 1).**

Table 1. Demographic and baseline characteristics of the enrolled patients

Parameters		**Total (N=3088)**
Gender#	Male	2176 (70.47%)
	Female	912 (29.53%)
Age(year)*		59.01 ± 11.99 (58.59 to 59.43)
Weight (kg)*		70.05 ± 11.69 (69.64 to 70.46)
Height (cm)*		163.05 ± 12.18 (162.62 to 163.48)
BMI (kg/m^2)*		26.41 ± 4.25 (26.26 to 26.56)
Comorbidities#	Hypertension	1539 (49.84%)
	Diabetes	1138 (36.85%)
	Cardiovascular diseases	411 (13.31%)
Follow-up Data Available	3 weeks	2490 (80.63%)
	6 weeks	598 (19.37%)
# Data presented as n (%) * Data presented as mean ± SD (95% CI)		

Presenting Complaints

Joint pain was the most common presenting complaint, reported by 69.8% of patients. Morning stiffness was observed in 26% of cases, followed by functional limitation (18.5%) and joint tenderness (18.2%). Fatigue was reported in 15.3% of patients, while joint swelling was noted in 10% of the study population **(Table 2).**

Table 2. Distribution of Presenting Complaints Among the Study Population

Presented complaints	**Total (N=3088)***
Joint pain	2155 (69.79%)
Morning stiffness	803 (26 %)
Functional limitation (difficulty walking, climbing stairs, squatting)	572 (18.52 %)
Joint tenderness	562 (18.20 %)
Fatigue	472 (15.29%)
Joint swelling	311 (10 %)
*Data presented n (%)	

Incidence of Adverse Events (AEs)

Out of 3,088 patients, treatment-related adverse events were infrequent. Nausea was reported in 43 patients (1.39%), vomiting in 31 patients (1.00%), abdominal pain in 21 patients (0.68%), headache in 17 patients (0.55%), and dizziness in 12 patients (0.39%). Overall, the incidence of adverse events was low and predominantly mild in nature.

Change in Pain Intensity

In patients who underwent 3 weeks of Polmacoxib treatment (n=2490), the mean pain intensity score decreased from a baseline value of 76.07±15.98 (95%CI: 75.44-76.70) to 32.44±11.28 at 3 weeks (95%CI: 31.90-32.78)**.** This corresponds to a mean reduction of 43.73 points in pain score (mean change -43.73± 13.99, 95%CI: -44.28 to -43.18), which was statistically significant compared to baseline ($p<0.05$) **(Figure 1)**. Further, for the patients who underwent for 6 weeks of Polmacoxib treatment (n=589), the mean pain intensity score showed a similar improvement. The mean score decreased from a baseline value of 77.37±17.65 (95%CI: 75.96-78.79) to 34.77±11.90 at 6 weeks (95%CI: 33.81-35.72). This corresponds to a mean reduction of 42.61 points from baseline (mean change: -42.61± 14.26, 95%CI: -43.75 to -41.47), which was also statistically significant compared to baseline ($p<0.05$) **(Figure 1)**.

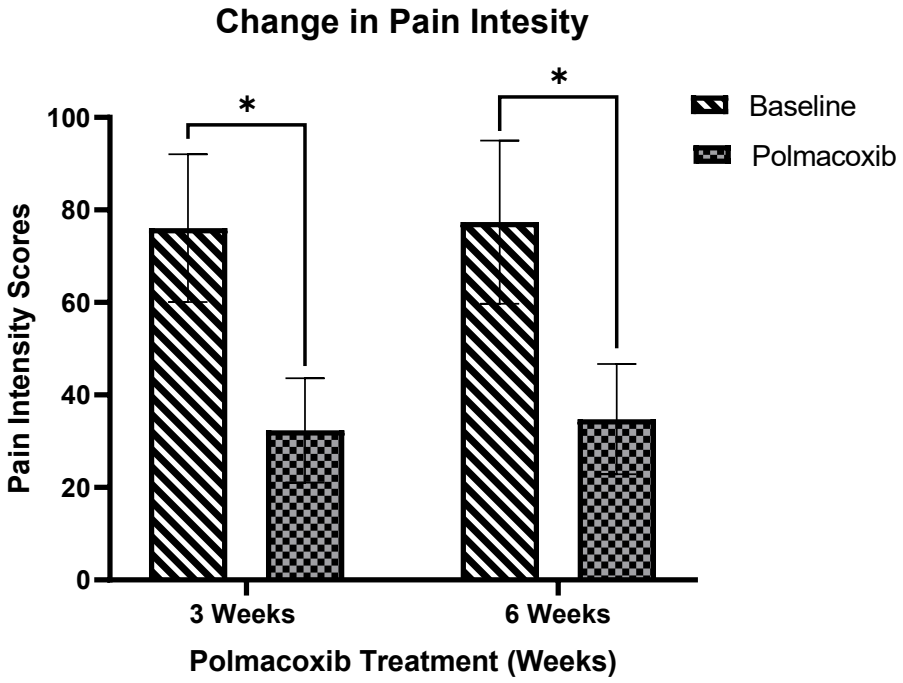

Figure 1. Changes in pain intensity scores among patients treated with Polmacoxib from Baseline to 3 and 6 Weeks. Bar graph depicting the mean pain intensity scores at baseline and after 3 or 6 weeks of polmacoxib therapy. Pain was assessed on a 0–100 scale, with higher scores indicating greater pain intensity. Error bars represent standard deviation. Data presented as mean ± SD (95% CI). *P value >0.05 (Wilcoxon signed-rank test).

DISCUSSION

The current retrospective study of 3088 OA patients provides real-world evidence that polmacoxib is an effective and well-tolerated alternative for managing OA-associated pain. Patients experienced a clinically significant improvement in pain intensity over the period of 3-6 weeks of therapy. These findings align with results from controlled trials, where polmacoxib (2 mg daily) reduced pain in OA patients, and the results were non-inferior to celecoxib (200 mg) and superior to placebo over 6 weeks of therapy (9). In these studies, polmacoxib reduced not only pain intensity but also stiffness and physical function to a magnitude comparable to celecoxib, suggesting that analgesics' benefits translated into better joint function (10). The degree of reduction in pain intensity mirrors its performance in a controlled trial. Real-world patients who often present varied complications and comorbidities, nonetheless achieved pain relief on the same level as that reported under controlled conditions, reinforcing the generalizability of polmacoxib's therapeutic effect.

Polmacoxib demonstrated a favorable safety profile in this large real-world cohort. Treatment-related adverse events were infrequent and primarily limited to mild gastrointestinal symptoms. No serious events, including gastrointestinal bleeding, cardiovascular complications, or renal impairment, were reported during the treatment period. The low incidence of side effects aligns with the expected safety advantages of a COX-2 selective NSAID, which minimizes COX-1 inhibition and thereby reduces gastrointestinal risk compared to traditional NSAIDs (11). From a cardiovascular safety perspective, the findings support the potential advantage of polmacoxib's dual mechanism. Its binding to carbonic anhydrase in cardiovascular tissues may reduce COX-2 inhibition in these areas, potentially minimizing pro-thrombotic effects and blood pressure elevation seen with earlier coxibs. Conversely, in inflamed joint tissues where COX-2 expression is high, the drug maintains strong anti-inflammatory activity. This tissue-selective action may explain the absence of observed cardiovascular events in this high-risk cohort during treatment (12). While this study is a 6-week observation period is too short to fully assess cardiovascular outcomes, the absence of any CV events and the stable tolerability in a comorbid population are encouraging signs that polmacoxib might cause a lower cardiovascular risk in real-world use. In this line of context, clinical studies of polmacoxib have reported no clinically significant GI events and an absence of blood pressure elevation during therapy (10,13). Notably, a recent prospective post-marketing study in India similarly found that only ~2% of polmacoxib-treated patients experienced any AEs, all of which were mild in intensity and deemed unrelated to polmacoxib, with no GI or cardiovascular events observed (14). The findings from this retrospective study corroborate these findings, where the minor GI disruption in about 1% of patients was infrequent and mild. Such evidence strongly indicates that polmacoxib offers a tolerability profile in routine care, addressing a key limitation of long-term NSAID therapy.

Notably, the study population reflects the diverse, comorbid patients commonly seen in routine OA practice, including elderly and overweight individuals with hypertension and diabetes. Such comorbidities often complicate NSAID therapy by increasing cardiovascular and gastrointestinal risks. The demonstrated efficacy and tolerability of polmacoxib in this real-world cohort suggest it may represent a valuable treatment option, even among higher-risk patient subgroups.

Despite favorable short-term outcomes, this study has a few limitations. As a retrospective, observational study without a placebo or active comparator, the study is inherently vulnerable to confounding and recording-related biases, and within-patient improvement may partly reflect non-specific effects that cannot be separated from treatment effects. Follow-up was short (primarily 3–6 weeks), limiting inference about long-term effectiveness and safety. Lastly, reliance on routine EHR documentation can underestimate adverse event frequency and may miss laboratory safety signals if labs are not systematically captured.

CONCLUSION

Overall, these real-world findings designate polmacoxib as an effective, well-tolerated short-term analgesic alternative in OA management, with substantial reduction in pain intensity and fewer recorded adverse events over 3-6 weeks. Future studies should prioritize studies where active comparator cohorts are included with longer follow-up to evaluate cv/renal outcomes and rare serious adverse events.

DECLARATION

Conflicts of interests: The authors declare no conflicts of interest.
Author contribution: All authors have contributed in the manuscript.
Author funding: Nill.

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