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# Nonprescription NSAIDs in Osteoarthritis: Clinical Insights on Naproxen Sodium for OA Pain Relief

*Naproxen Sodium, branded as Aleve®, temporarily reduces fever and temporarily relieves minor aches and pains due to minor pain of arthritis, muscular aches, backache, menstrual cramps, headache, toothache, and the common cold. Use as directed.<sup>1</sup>*

**OSTEOARTHRITIS (OA) IS THE MOST** prevalent form of arthritis, affecting an estimated 33 million adults in the US and particularly those over 45 years old.<sup>2</sup> Characterized by the progressive degeneration of articular cartilage and associated joint structures, OA leads to pain, stiffness, swelling, and impaired function.<sup>3</sup> Emerging evidence also highlights the role of low-grade inflammation in driving structural progression, accelerating cartilage loss, and worsening joint damage over time.<sup>4</sup> Despite being more common with age, OA is not an inevitable consequence of aging.<sup>2</sup> Evidence-based interventions—both pharmacologic and nonpharmacologic—can help prevent or delay disease progression and improve quality of life.<sup>2</sup>

Pharmacists often serve as frontline health care providers for patients with OA, offering education on self-care strategies and guiding appropriate use of over-the-counter (OTC) pain relief options.

## OA PAIN RELIEF OPTIONS

Pain related to OA can interfere with daily activities and functioning.<sup>3</sup> Nonprescription pain relievers can provide relief for OA pain.

Although OA has no cure, its symptoms can be effectively managed with a multimodal approach that includes regular physical activity, weight management, joint protection strategies, and pharmacologic treatment when appropriate.<sup>2</sup> When medications for pain relief are warranted, major OA guidelines consistently recommend nonopioid therapies as first-line options, with NSAIDs such as Aleve cited as effective agents. The American Academy of Orthopedic Surgeons strongly recommends NSAIDs for pain relief for knee OA, while the American College of Rheumatology strongly recommends NSAIDs for knee, hip, and hand OA.<sup>5,6</sup>

## COMPARING OTC ANALGESICS

To relieve OA pain, OTC analgesics including NSAIDs (eg, Aleve, ibuprofen), and non-NSAIDs (eg, acetaminophen) are available. Each option has distinct mechanisms, dosing regimens, and durations of action that affect efficacy, tolerability, and convenience (**Table 1**).<sup>1,7,8</sup>

NSAIDs relieve pain by inhibiting cyclooxygenase (COX) enzymes, which reduce the production of eicosanoids involved in platelet adhesion, vasodilation, temperature regulation, and pain perception. In contrast, although the actual mechanism of action is unknown, acetaminophen is thought to act primarily in the central nervous system. For long-lasting pain relief, Naproxen Sodium, an NSAID, provides up to 12 hours of pain relief with 1 dose.<sup>9</sup>

## EFFICACY OF ALEVE® (NAPROXEN SODIUM)

Study data support the efficacy and safety of Aleve in relieving OA pain, bolstering its role as a therapeutic option of choice for long-lasting pain relief.<sup>10-12</sup>

### Aleve vs Ibuprofen for OA Knee Pain

In 2 identical, multicenter, randomized, double-blind, placebo-controlled studies, the efficacy and safety of Aleve were evaluated in adults 25 years and older with knee OA using aged-based dosing (age < 65 years, 660 mg/day; age ≥ 65 years, 440 mg/day) comparing outcomes to ibuprofen (1200 mg/day) and placebo. Among the 461 enrolled participants, both Aleve® (naproxen sodium) and ibuprofen effectively relieved mild to moderate knee OA pain over the 7-day period. Notably, Aleve showed greater efficacy in reducing night pain on days 1, 2, 3, and 5 ( $P < .05$  for nights 1 and 3;  $P < .01$  for nights 2 and 5), whereas ibuprofen showed significantly greater efficacy only on nights 1 and 2 ( $P < .05$ ).<sup>10</sup>

**TABLE 1.** Comparison of OTC Analgesics<sup>1,7,8</sup>

Attribute	Aleve	Ibuprofen	Acetaminophen Extra Strength
Dosing frequency	Every 8 to 12 hours	Every 4 to 6 hours	Every 6 hours
Maximum OTC daily dose	660 mg	1200 mg	4000 mg
Duration of action	Up to 12 hours	Up to 6 hours	Up to 6 hours

OTC, over-the-counter.

## Aleve vs Placebo

In a post hoc pooled analysis of 4 randomized, double-blind, placebo-controlled studies (NCT03570554), Aleve was evaluated in patients with OA using age-based dosing (age < 65 years, 660 mg/day; age ≥ 65 years, 440 mg/day) over 7 days. Key assessments—including pain severity and physical function—were measured using 5-point rating scales and timed walking tests. Compared to placebo, Aleve improved pain relief and physical function ( $P < .05$ ).<sup>11</sup>

## ADDITIONAL SUPPORT FOR USE OF NSAIDS IN OA PAIN

### Network Meta-Analysis of OA Treatment Options

A network meta-analysis of 137 randomized controlled trials involving over 33,000 adults with knee OA assessed the comparative efficacy of pharmacologic treatments. Across outcomes of pain, function, and stiffness at 3-month follow-up, NSAIDs like naproxen significantly outperformed oral placebo and showed greater efficacy than acetaminophen. Its effectiveness in managing pain was comparable to that of other NSAIDs, including ibuprofen, diclofenac, and celecoxib.<sup>12</sup>

## SAFETY AND TOLERABILITY CONSIDERATIONS

NSAIDs are widely used for OA pain relief, but they carry potential risks that must be carefully balanced against their benefits—particularly in older adults or patients with comorbid conditions. Aleve for short-term pain management is safe when used as directed.<sup>1</sup> A pooled analysis of 8 multiple-dose, randomized controlled trials in OA with fixed dosing regimens of 7 days or longer demonstrated that short-term use of nonprescription doses of Aleve is associated with a safety profile comparable to placebo across age groups, including older populations.<sup>13</sup>

Gastrointestinal (GI) complications are among the most well-known adverse effects of NSAID use. These may include mucosal irritation, peptic ulcers, GI bleeding, and, in severe cases, perforation. The risk is heightened in individuals with a history of GI disorders, those older than 65 years, and patients using concomitant antiplatelet therapies.<sup>14</sup>

Cardiovascular (CV) risks also merit careful consideration. All NSAIDs should be used cautiously in patients with established CV disease or significant CV risk factors.

## PHARMACISTS' ROLE IN OPTIMIZING OA PAIN MANAGEMENT

The extended duration of action and reduced dosing

frequency of Aleve, coupled with its efficacy and safety profiles, make it a valuable OTC option for relieving OA pain, particularly when aligned with guideline-based recommendations. Pharmacists are well positioned to optimize its use by assessing patient-specific factors—such as comorbidities, concurrent medications, and prior treatment responses—and by counseling on appropriate dosing and potential risks. A pharmacist's essential role in the broader continuum of OA care is reinforced by timely referrals when a patient's symptoms persist or worsen. Through targeted education and ongoing communication, pharmacists can help bridge the gap between evidence-based guidance and real-world adherence. 🌐

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