Survey Report

Role of NSAIDs in Management of Osteoarthritis and Rheumatoid Arthritis

Version No.: 1.1

The study was conducted according to the approved protocol and in compliance with the protocol, Good Clinical Practice (GCP), and other applicable local regulatory requirements.

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1 INTRODUCTION

Rheumatic disorders include a wide range of conditions that mainly affect the joints, muscles, and connective tissues, causing pain, inflammation, and gradual joint damage. Two of the most prevalent and recognized forms of rheumatic disorders are osteoarthritis (OA) and rheumatoid arthritis (RA) [1]. OA is a degenerative inflammatory joint condition that mainly affects older individuals, resulting in significant socioeconomic impacts on health and social-care systems. It is considered a disease of the entire joint, with changes occurring in the articular cartilage, subchondral bone, ligaments, and synovium [2]. RA is a severe, chronic, and progressive autoimmune disease characterized by inflammation of the synovium. It affects diarthrodial joints, such as those in the hands, knees, and hips, leading to systemic complications, joint and bone destruction, and increasing disability over time [3].

NSAIDs (Nonsteroidal Anti-Inflammatory Drugs) are commonly used to alleviate pain, reduce fever, and address inflammatory conditions. This summary covers their uses, mechanisms, administration methods, side effects, contraindications, monitoring requirements, and key points for healthcare providers.

NSAIDs are FDA-approved for their antipyretic (fever-reducing), anti-inflammatory, and analgesic (pain-relieving) properties. They are effective for treating muscle pain, menstrual cramps, arthritis, fever, gout, migraines, and can serve as alternatives to opioids in managing certain acute injuries. These medications are classified based on their chemical structure and selectivity: acetylated salicylates (aspirin), non-acetylated salicylates (diflunisal, salsalate), propionic acids (naproxen, ibuprofen), acetic acids (diclofenac, indomethacin), enolic acids (meloxicam, piroxicam), anthranilic acids (meclofenamate, mefenamic acid), naphthylalanine (nabumetone), and selective COX-2 inhibitors (celecoxib, etoricoxib). Additionally, topical NSAIDs like diclofenac gel are available for treating conditions such as acute tenosynovitis, ankle sprains, and soft tissue injuries.

NSAIDs primarily work by inhibiting the enzyme cyclooxygenase (COX), which is necessary for converting arachidonic acid into thromboxanes, prostaglandins, and prostacyclins. The reduction of these eicosanoids accounts for the

therapeutic benefits of NSAIDs. Thromboxanes are involved in platelet adhesion, prostaglandins in vasodilation and fever regulation, and prostacyclins in pain relief.

There are two isoenzymes of cyclooxygenase: COX-1 and COX-2. COX-1 is continuously present in the body and is vital for protecting the gastrointestinal mucosa, maintaining kidney function, and aiding platelet aggregation. COX-2, on the other hand, is produced during inflammatory responses. Most NSAIDs are nonselective and inhibit both COX-1 and COX-2, but COX-2 selective NSAIDs (e.g., celecoxib) specifically target COX-2, resulting in a different side effect profile. Because COX-1 is crucial for gastric mucosal integrity and COX-2 is mainly involved in inflammation, COX-2 selective NSAIDs can provide anti-inflammatory benefits without compromising the gastric mucosa.

Therefore, understanding the prescribing patterns and preferences of physicians regarding the use of NSAIDs in the management of OA and RA is crucial for optimizing treatment strategies and minimizing associated risks.

2 RATIONALE OF THE STUDY

The study aimed to gather comprehensive insights into the clinical use of NSAIDs in managing pain associated with osteoarthritis (OA) and rheumatoid arthritis (RA). By understanding prescribing patterns, treatment preferences, and perceived efficacy among physicians, the study sought to optimize therapeutic strategies and improve patient outcomes.

The purpose of the study was to assess current clinical practices and preferences of physicians regarding NSAID use in OA and RA management. Specifically, the study aimed to explore factors that influenced NSAID selection, such as efficacy, safety considerations, and pharmacological profiles. The goal was to provide evidence-based recommendations aimed at enhancing treatment outcomes based on these insights.

3 STUDY OBJECTIVE

The primary objective of this study is to assess the prescribing patterns and preferences of physicians regarding the use of NSAIDs in the management of OA and RA.

4 METHODS

This study employed a cross-sectional, questionnaire-based design to assess prescribing patterns and preferences of Indian physicians regarding the use of NSAIDs in managing osteoarthritis (OA) and rheumatoid arthritis (RA).

The target population comprised physicians practicing in India who manage patients with OA and RA. Participants were recruited through professional networks and medical associations known to engage in the treatment of these conditions. Physicians were identified and invited to participate via email or professional network announcements. Prior to participation, detailed information regarding the study's objectives, procedures, and confidentiality measures was provided to potential participants.

A structured questionnaire consisting of 10 questions was developed to gather data on physicians' clinical experience, prescribing practices, and perceptions of NSAID use in OA and RA management. The questionnaire was administered electronically to facilitate efficient data collection and ensure uniformity in responses.

Responses to the survey were collected electronically using a secure platform to maintain participant anonymity and data confidentiality. Completed surveys were stored securely in compliance with applicable data protection regulations.

Statistical analysis was conducted to summarize survey findings and identify key trends in prescribing patterns and preferences among participating physicians. Descriptive statistics were used to present frequencies and percentages of responses.

A target sample size of 100 Indian physicians was selected to ensure the study's findings were based on a diverse and representative sample. This sample size was deemed adequate to support meaningful statistical analysis and draw

reliable conclusions regarding the use of NSAIDs in OA and RA management among Indian healthcare providers.

Study results were compiled into a comprehensive report detailing key findings and implications for clinical practice. Findings were intended for dissemination through scientific publication in peer-reviewed journals and presentation at relevant medical conferences, subject to suitability and acceptance by respective venues.

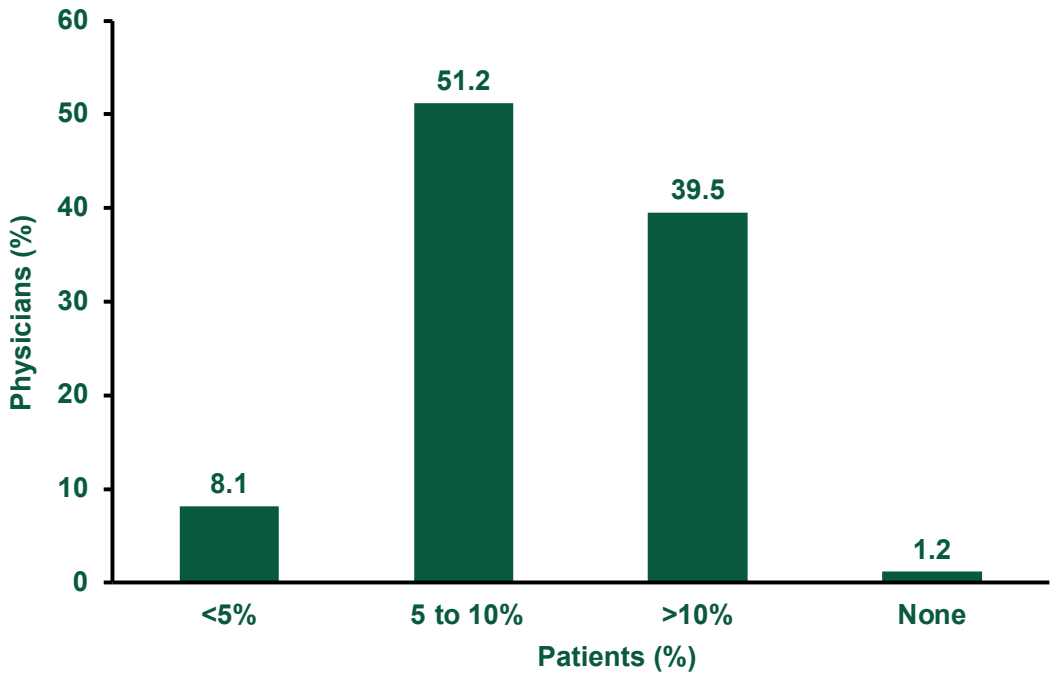
This study adhered to the ethical principles outlined in the Declaration of Helsinki. Ethical approval was sought from an Independent Ethics Committee. Participants were assured of their right to withdraw from the study at any time without any consequences. All responses were anonymized to ensure participant confidentiality.

5 RESULTS

A total of 86 HCPs participated in the survey. Below is the summary of the responses.

Question 1: How many patients suffering from pain do you see in your daily clinical practice?

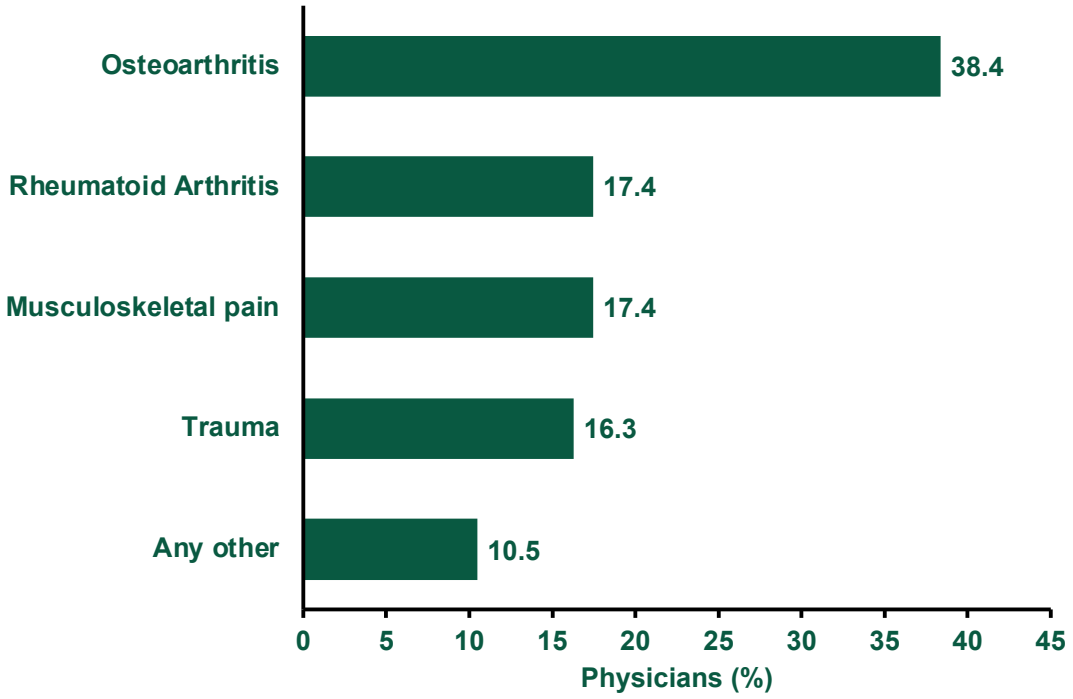
Options	Number of Physicians (N=86)
<5%	7 (8.1)
5 to 10 %	44 (51.2)
>10%	34 (39.5)
None	1 (1.2)
Data presented as n (%)	



- The majority of physicians (51.2%) see 5 to 10% of their patients suffering from pain in their daily clinical practice.
- A significant portion (39.5%) see more than 10% of their patients with pain issues.
- A small group (8.1%) sees less than 5% of their patients with pain, and only one physician (1.2%) reported not seeing any patients suffering from pain.

Question 2: What is the most common cause of pain presenting in your clinic?

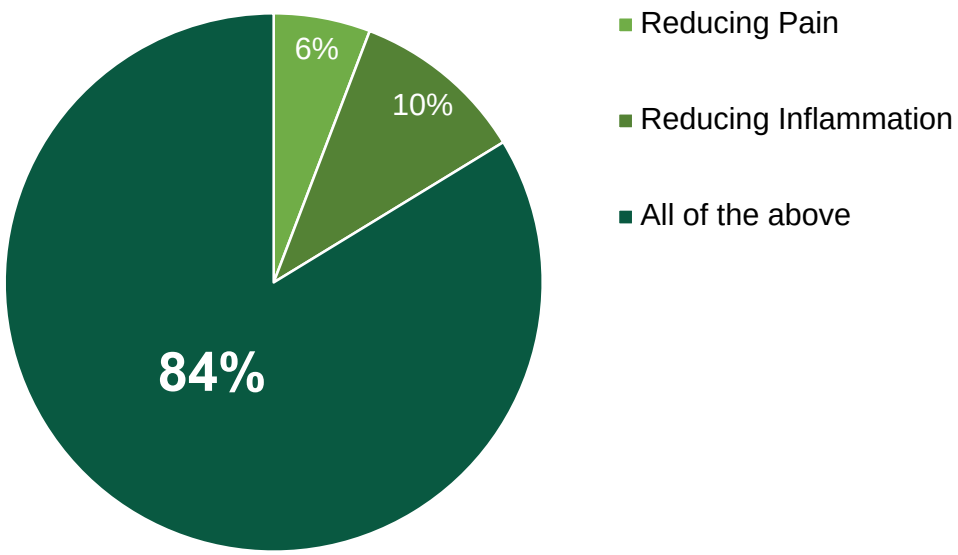
Options	Number of Physicians (N=86)
Osteoarthritis	33 (38.4)
Rheumatoid Arthritis	15 (17.4)
Musculoskeletal pain	15 (17.4)
Trauma	14 (16.3)
Any other	9 (10.5)
Data Presented as n (%).	



- The most common cause of pain presenting in clinics is osteoarthritis, reported by 38.4% of physicians.
- Both rheumatoid arthritis and musculoskeletal pain are equally common, each cited by 17.4% of physicians.
- Trauma is reported by 16.3% of physicians as the most common cause, while 10.5% of physicians cited other causes.

Question 3: In your opinion, in patients with OA and RA NSAIDs provide relief by –

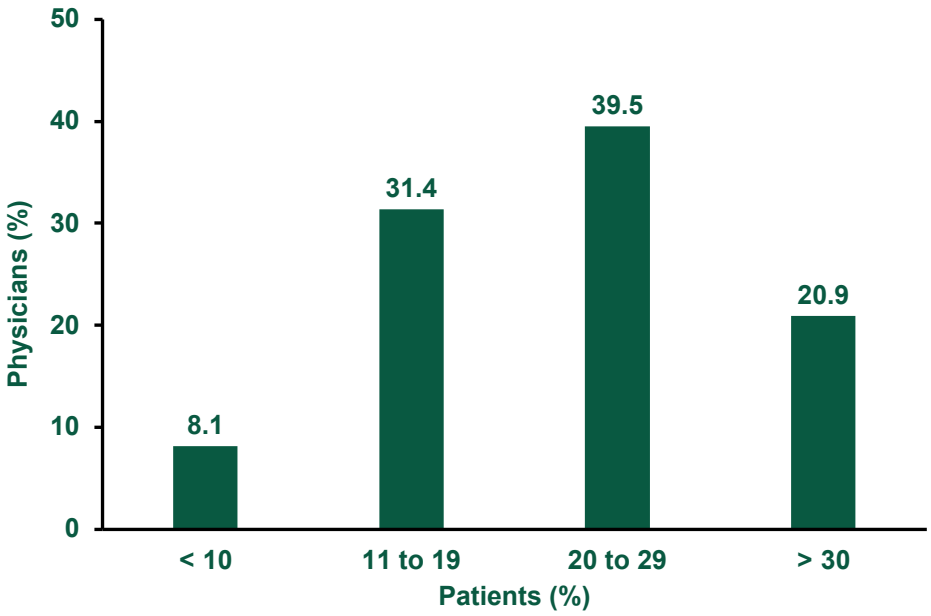
Options	Number of Physicians (N=86)
Reducing Pain	5 (5.8)
Reducing Inflammation	9 (10.5)
All of the above	72 (83.7)
Data Presented as n (%).	



- The majority of physicians (83.7%) believe that NSAIDs (Nonsteroidal Anti-Inflammatory Drugs) provide relief in patients with osteoarthritis (OA) and rheumatoid arthritis (RA) by both reducing pain and reducing inflammation.
- A smaller portion of physicians (10.5%) think that NSAIDs provide relief primarily by reducing inflammation.
- Only a minimal number of physicians (5.8%) feel that the primary relief from NSAIDs comes solely from reducing pain.
- These results highlight the consensus among physicians that NSAIDs have a dual role in managing symptoms of OA and RA, addressing both pain and inflammation effectively.

Question 4: In your clinical practice, how many patients of Osteoarthritis (OA) do you treat in a week?

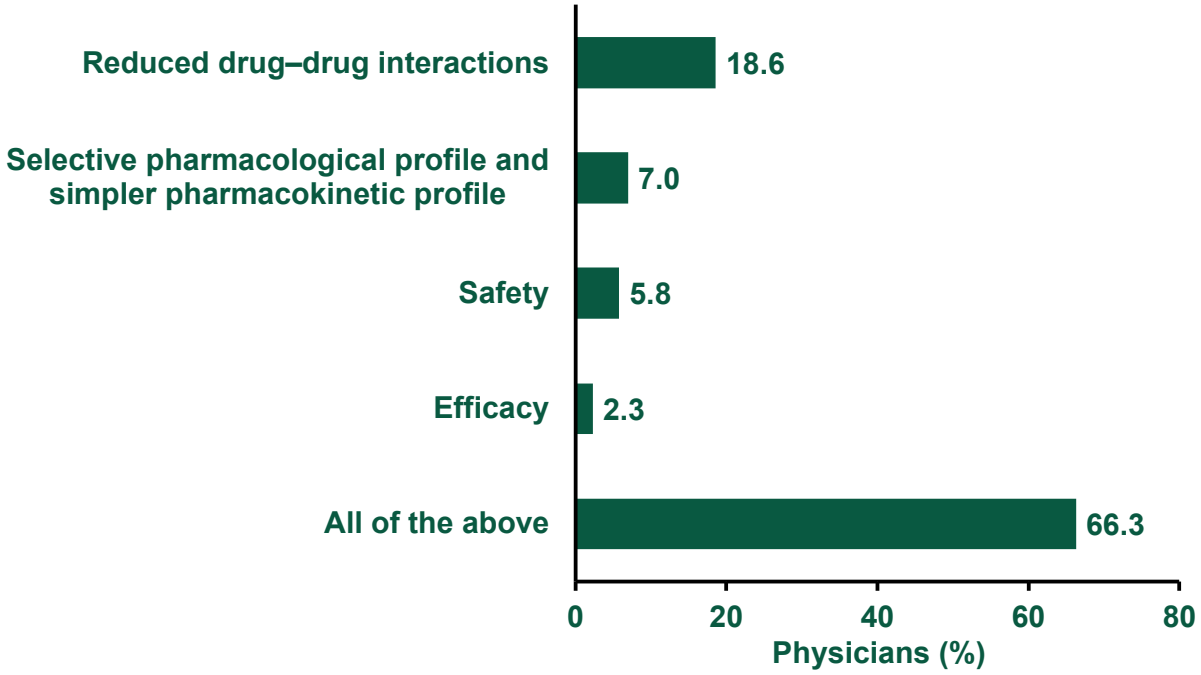
Options	Number of Physicians (N=86)
< 10	7 (8.1)
11 to 19	27 (31.4)
20 to 29	34 (39.5)
> 30	18 (20.9)
Data Presented as n (%).	



- The majority of physicians (39.5%) treat between 20 to 29 osteoarthritis (OA) patients per week.
- This is followed by 31.4% of physicians who see between 11 to 19 OA patients weekly.
- A significant portion (20.9%) of physicians manage over 30 OA patients in a week.
- A smaller group, 8.1%, treat fewer than 10 OA patients weekly.
- These results indicate a substantial workload related to osteoarthritis management in clinical practice, with the highest percentage of physicians treating 20 to 29 patients each week.

Question 5: What attributes do you keep in mind during selection of NSAIDs in patients with OA?

Options	Number of Physicians (N=86)
Reduced drug–drug interactions	16 (18.6)
Selective pharmacological profile and simpler pharmacokinetic profile	6 (7.0)
Safety	5 (5.8)
Efficacy	2 (2.3)
All of the above	57 (66.3)
Data Presented as n (%).	

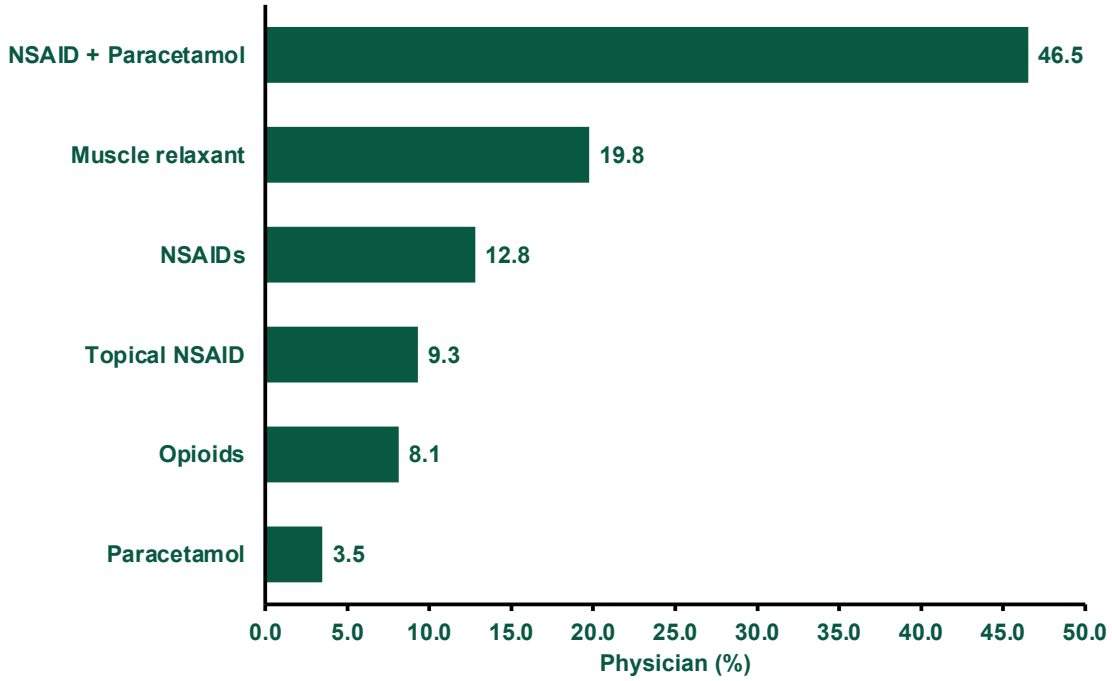


- The majority of physicians (66.3%) consider all the listed attributes—reduced drug–drug interactions, selective pharmacological profile and simpler pharmacokinetic profile, safety, and efficacy—when selecting NSAIDs for patients with osteoarthritis (OA).
- A significant portion of physicians (18.6%) prioritize reduced drug–drug interactions.

- Selective pharmacological profile and simpler pharmacokinetic profile are important for 7.0% of physicians, while safety is a key consideration for 5.8%. Only 2.3% of physicians primarily focus on efficacy.
- These results highlight the multifaceted approach that most physicians take in selecting NSAIDs for OA, valuing a combination of reduced interactions, pharmacological properties, safety, and efficacy.

Question 6: As per your clinical expertise, what should be the 1st line treatment for the management of pain?

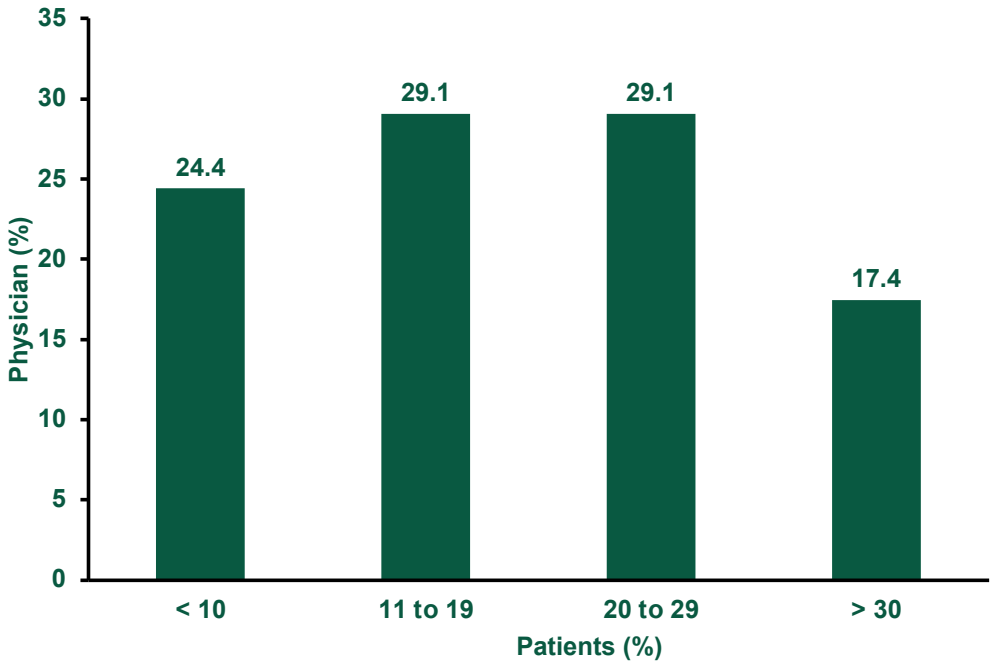
Options	Number of Physicians (N=86)
NSAID + Paracetamol	40 (46.5)
Muscle relaxant	17 (19.8)
NSAIDs	11 (12.8)
Topical NSAID (Topical analgesic gel/Spray)	8 (9.3)
Opioids	7 (8.1)
Paracetamol	3 (3.5)
Data Presented as n (%).	



- The majority of physicians (46.5%) recommend a combination of NSAID and Paracetamol as the first-line treatment for managing pain.
- Muscle relaxants are the second most common choice, preferred by 19.8% of physicians.
- Standalone NSAIDs are recommended by 12.8% of physicians, while topical NSAIDs (in the form of gels or sprays) are chosen by 9.3%.
- Opioids are selected by 8.1% of physicians, and a smaller percentage (3.5%) suggest Paracetamol as the first-line treatment.
- These results indicate a strong preference for combination therapy with NSAID and Paracetamol among physicians for the initial management of pain, reflecting the importance of both analgesic and anti-inflammatory effects in treatment.

Question 7: In your clinical practice, how many patients of rheumatoid Arthritis do you treat in a week?

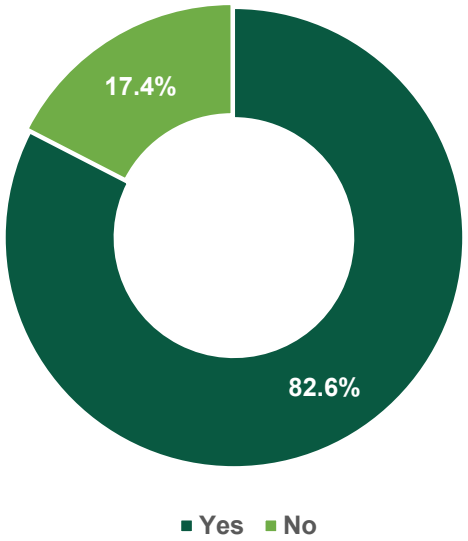
Options	Number of Physicians (N=86)
<10	21 (24.4)
11 to 19	25 (29.1)
20 to 29	25 (29.1)
>30	15 (17.4)
Data Presented as n (%).	



- In clinical practice, the number of rheumatoid arthritis (RA) patients treated weekly varies among physicians.
- 29.1% of physicians treat between 11 to 19 RA patients weekly, and another 29.1% see between 20 to 29 RA patients weekly.
- 24.4% of physicians manage fewer than 10 RA patients each week, while 17.4% handle more than 30 RA patients per week.
- These results indicate that the majority of physicians treat a moderate number of RA patients weekly, with a significant number managing between 11 to 29 patients.
- A smaller group treats fewer than 10 or more than 30 RA patients weekly.

Question 8: In your clinical practice do you prefer unichiral NSAIDS over NSAIDS for pain management?

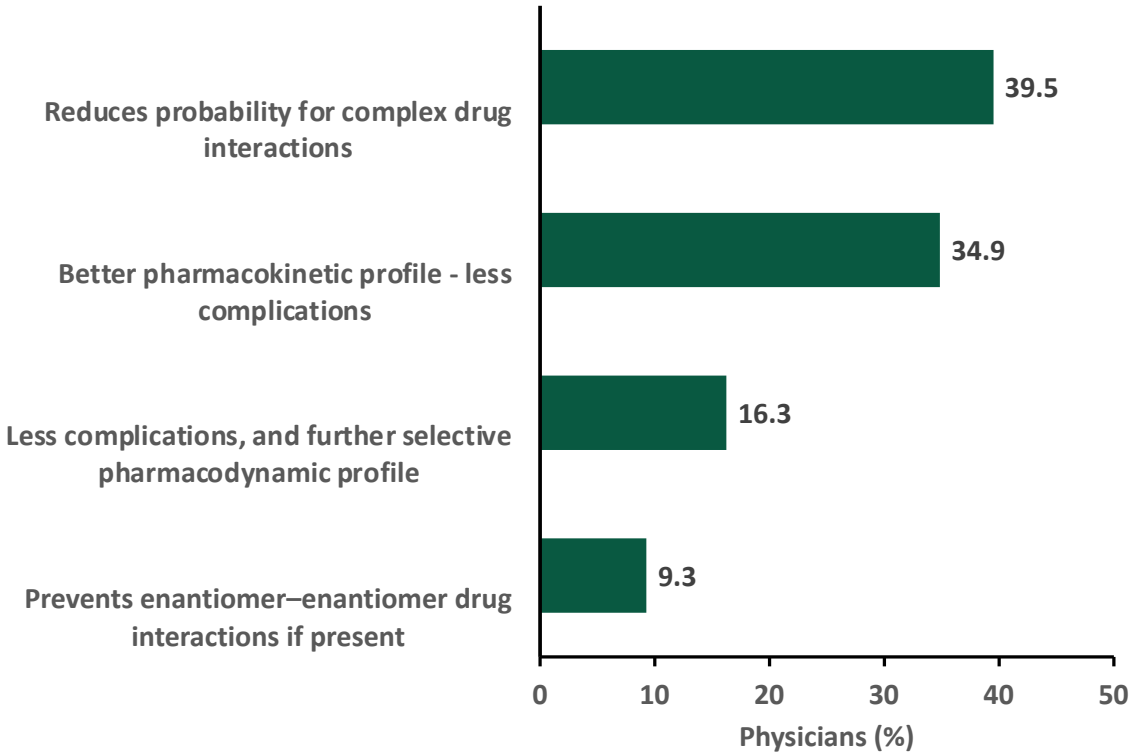
Options	Number of Physicians (N=86)
Yes	71 (82.6)
No	15 (17.4)
Data Presented as n (%).	



- In clinical practice, a significant majority of physicians (82.6%) prefer unichiral NSAIDs over regular NSAIDs for pain management.
- A smaller portion (17.4%) do not prefer unichiral NSAIDs.
- This indicates a strong preference among physicians for the use of unichiral NSAIDs in managing pain.

Question 9: As per your clinical experience what are the advantages of unichiral NSAIDS?

Options	Number of Physicians (N=86)
Reduces probability for complex drug interactions	34 (39.5)
Better pharmacokinetic profile - less complications	30 (34.9)
Less complications, and further selective pharmacodynamic profile	14 (16.3)
Prevents enantiomer–enantiomer drug interactions if present	8 (9.3)
Data Presented as n (%).	

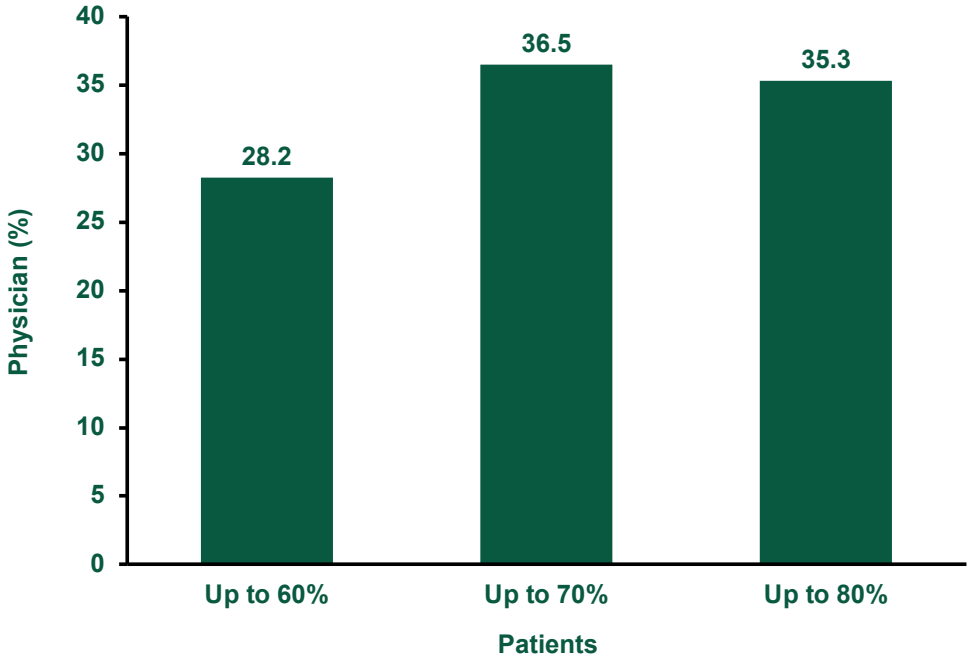


In clinical experience, physicians cite several advantages of unichiral NSAIDs:

- This advantage is noted by 39.5% of physicians, making it the most frequently cited benefit. It suggests that unichiral NSAIDs can simplify drug regimens and potentially reduce adverse interactions with other medications.
- 34.9% of physicians believe unichiral NSAIDs have a superior pharmacokinetic profile, leading to fewer complications. This indicates an advantage in the drug's absorption, distribution, metabolism, and excretion processes.
- 16.3% of physicians appreciate that unichiral NSAIDs have fewer complications and a more selective pharmacodynamic profile, which pertains to the drug's effects on the body and its mechanisms of action.
- 9.3% of physicians recognize that unichiral NSAIDs prevent interactions between different enantiomers (mirror-image forms of a molecule), which can be beneficial in ensuring consistent drug efficacy and safety.
- These results highlight the perceived benefits of unichiral NSAIDs in clinical practice, particularly in reducing drug interactions and complications due to better pharmacokinetic and pharmacodynamic profiles.

Question 10: How much reduction in pain intensity do you see with S-Etodolac tablets in patients with OA?

Options	Number of Physicians (N=85)
Up to 60%	24 (28.2)
Up to 70%	31 (36.5)
Up to 80%	30 (35.3)
Data Presented as n (%).	



- Around 28.2% of physicians (24 respondents) reported that the medication could reduce pain intensity by up to 60%.
- A larger proportion, 36.5% (31 physicians), believed that pain relief could reach up to 70%, while 35.3% (30 physicians) anticipated reductions of up to 80%.
- Overall, these findings suggest that S-Etodolac is widely regarded as an effective treatment option for managing OA-related pain, with a significant number of physicians expecting substantial levels of pain reduction.

6 SUMMARY

This survey of physicians revealed that over half (51.2%) see 5 to 10% of their patients suffering from pain, with 39.5% encountering more than 10% of patients with pain-related issues. Osteoarthritis (OA) is the most common cause of pain, reported by 38.4% of physicians, followed by rheumatoid arthritis (RA) and musculoskeletal pain (17.4% each), and trauma (16.3%).

Most physicians (83.7%) believe NSAIDs effectively manage pain and inflammation in OA and RA, with 39.5% treating 20 to 29 OA patients weekly. In selecting NSAIDs, 66.3% consider multiple factors, emphasizing reduced drug–drug interactions and pharmacological profiles. The first-line treatment often recommended is a combination of NSAIDs and Paracetamol (46.5%), followed by muscle relaxants (19.8%).

Regarding RA management, 29.1% of physicians treat between 11 to 19 or 20 to 29 patients weekly. A significant majority (82.6%) prefer unichiral NSAIDs for pain management due to their perceived benefits, such as reducing drug interactions and having superior pharmacokinetic profiles. Most physicians believe S-Etodolac can reduce pain intensity significantly, with expectations ranging from 60% to 80%.

7 DISCUSSION

The findings underscore the substantial burden of pain management faced by physicians in daily practice, with a majority reporting that a significant portion of their patient population suffers from various pain conditions. The prevalence of osteoarthritis as the leading cause of pain highlights the need for effective treatment strategies in this demographic.

Physicians' consensus on the dual role of NSAIDs in alleviating both pain and inflammation in conditions like OA and RA reflects a comprehensive understanding of the therapeutic needs in managing these chronic conditions. The preference for combination therapy, particularly with NSAIDs and Paracetamol, aligns with clinical guidelines emphasizing a multifaceted approach to pain relief, leveraging both analgesic and anti-inflammatory properties for optimal outcomes.

The significant workload associated with osteoarthritis management, with nearly 40% of physicians treating 20 to 29 OA patients weekly, indicates a critical need for effective treatment options and potential policy adjustments to support healthcare providers in this demanding field.

When selecting NSAIDs, physicians prioritize attributes that minimize potential drug interactions and optimize pharmacological profiles. This approach underscores the complexity of managing patients with comorbidities, as many OA patients may be on multiple medications. The emphasis on a broader set of factors beyond efficacy demonstrates a holistic approach to patient care.

The strong preference for unichiral NSAIDs reflects a growing awareness of their potential advantages over traditional NSAIDs. By simplifying drug regimens and minimizing adverse interactions, unichiral NSAIDs can enhance patient safety and treatment efficacy. The noted pharmacokinetic and pharmacodynamic benefits further support their increasing utilization in clinical practice.

Physicians' expectations regarding pain reduction with S-Etodolac indicate a positive outlook on its efficacy in managing OA-related pain, with substantial reductions anticipated by the majority. This optimism highlights the need for continued research and education surrounding the use of new and existing pain management therapies to ensure that physicians are equipped with the best options for their patients.

In conclusion, the results reveal a comprehensive picture of current practices and beliefs among physicians regarding pain management in OA and RA, emphasizing the importance of tailored treatment strategies that consider both efficacy and patient safety.

8 CLINICAL RECOMMENDATIONS

- Physicians should adopt a multifaceted approach to pain management, combining NSAIDs with other therapeutic options such as Paracetamol and muscle relaxants to address both pain and inflammation effectively.
- Select NSAIDs with a favorable safety profile, reduced drug–drug interactions, and a simpler pharmacokinetic profile to minimize complications, especially in patients with multiple comorbidities.
- Regularly monitor patients for side effects and efficacy of pain management therapies, particularly those on long-term NSAID treatment, to ensure optimal outcomes and timely adjustments.
- Consider the use of unichiral NSAIDs for their superior pharmacokinetic and pharmacodynamic profiles, which can reduce drug interactions and enhance patient safety.
- Educate patients about the benefits and potential side effects of their pain management regimen, encouraging adherence and timely reporting of adverse effects.

9 CONSULTANT OPINION

Based on the survey results, the consensus among physicians is that a combination of NSAIDs and other analgesics like Paracetamol is the most effective first-line treatment for managing pain in conditions such as osteoarthritis and rheumatoid arthritis. The strong preference for unichiral NSAIDs suggests they are perceived as safer and more effective due to fewer drug interactions and better pharmacokinetic properties. Physicians believe that these medications significantly reduce pain intensity, which supports their use as a primary treatment option.

10 MARKET OPPORTUNITIES

- Invest in the research and development of new unichiral NSAIDs that offer improved safety profiles and efficacy. Highlight their benefits in marketing campaigns to differentiate them from traditional NSAIDs.
- Create combination therapy products that include NSAIDs and Paracetamol, targeting the large market of patients with osteoarthritis and rheumatoid arthritis. Ensure these products are convenient and easy to use to enhance patient adherence.
- Develop educational programs for healthcare providers to raise awareness about the benefits of unichiral NSAIDs and combination therapies, potentially increasing their adoption in clinical practice.
- Implement patient support programs that provide information on pain management, medication adherence, and monitoring, which can improve treatment outcomes and patient satisfaction.

11 MARKET POSITIONING

- Position unichiral NSAIDs as the safer and more effective option for pain management in chronic conditions like osteoarthritis and rheumatoid arthritis. Emphasize their superior pharmacokinetic and pharmacodynamic profiles in marketing materials.
- Market combination therapy products as offering comprehensive pain relief by addressing both pain and inflammation, appealing to both physicians and patients looking for effective treatment solutions.
- Highlight the patient-centric benefits of new pain management products, such as reduced side effects, fewer drug interactions, and improved quality of life, to differentiate from competitors.
- Position your brand as a leader in pain management innovation by showcasing ongoing research and development efforts aimed at creating safer and more effective therapies for chronic pain conditions.

12 REFERENCES

1) Carrión M, Frommer KW, Pérez-García S, Müller-Ladner U, Gomariz RP, Neumann E. The Adipokine Network in Rheumatic Joint Diseases. Int J Mol Sci. 2019;20(17):4091.
2) Martel-Pelletier J, Barr AJ, Cicuttini FM, Conaghan PG, Cooper C, Goldring MB, et al. Osteoarthritis. Nat Rev Dis Primers. 2016;2:16072.
3) Smolen JS, Aletaha D, Barton A, Burmester GR, Emery P, Firestein GS, et al. Rheumatoid arthritis. Nat Rev Dis Primers. 2018;4:18001.