

Original Research Article

A cross-sectional survey assessing clinical utilization and physician perspectives on PEA-based therapy in the management of neuropathic pain

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ABSTRACT

Background: Neuropathic pain is a chronic condition associated with substantial morbidity and impaired quality of life. Palmitoylethanolamide (PEA), an endogenous lipid mediator with anti-inflammatory and neuroprotective properties, has emerged as a potential adjunctive therapy for neuropathic pain. This survey evaluated physicians' utilization patterns, therapeutic positioning, perceived effectiveness, and safety of PEA-based formulations in routine clinical practice.

Methods: A descriptive, questionnaire-based cross-sectional survey was conducted among orthopedic surgeons attending IOACON-2025, Guwahati, India. A structured nine-item questionnaire was administered electronically, and responses from 93 physicians were analyzed using descriptive statistics.

Results: Most physicians reported frequent (49.5%) or very frequent (9.7%) prescribing of PEA-based formulations. Neuropathic pain (71.0%), chronic low back pain (60.2%), and peripheral nerve injury (57.0%) were the most common indications. More than half of the respondents (60.2%) initiated PEA-based therapy as an early adjunct to first-line treatment, while 26.9% prescribed it following an inadequate response to gabapentinoids. Overall efficacy was rated as highly effective by 24.7% and moderately effective by 69.9% of physicians. Symptom improvement was observed within 1-2 weeks by 40.9% of respondents and within 2-4 weeks by 30.1%. PEA-based formulations were considered highly or moderately effective in improving pain, burning sensation, tingling, paresthesia, and sleep disturbances by 94.6% of physicians. Most respondents (83.9%) reported excellent tolerability with minimal adverse effects. Once-daily dosing and improved patient compliance were identified as the most important factors influencing prescribing preference. Additionally, 94.6% considered PEA-based formulations suitable for routine or selective long-term maintenance therapy.

Conclusions: PEA-based formulations are widely utilized in clinical practice and are perceived by physicians as effective, well tolerated, and suitable for both adjunctive and long-term management of neuropathic pain. These findings support the growing role of PEA-based therapy in contemporary neuropathic pain management.

Keywords: Neuroinflammation, Chronic pain management, Prescribing patterns

INTRODUCTION

Neuropathic pain is a chronic and often debilitating condition resulting from a lesion or disease affecting the somatosensory nervous system. It is characterized by

symptoms such as spontaneous pain, burning sensation, tingling, paresthesia, allodynia, and hyperalgesia, which significantly impair quality of life, sleep, daily functioning, and psychological well-being. The global prevalence of neuropathic pain is estimated to range

between 6.9% and 10%, making it a substantial public health concern with considerable socioeconomic burden.^{1,2} Unlike nociceptive pain, which arises from tissue injury and inflammation, neuropathic pain results from pathological alterations in neural signaling pathways, leading to persistent pain perception even in the absence of ongoing tissue damage. Clinically, it is characterized by a spectrum of sensory symptoms including spontaneous pain, burning sensations, electric shock-like pain, tingling, paresthesia, dysesthesia, allodynia, and hyperalgesia. These symptoms frequently coexist and can vary in intensity, making diagnosis and management particularly challenging.^{3,4}

Neuropathic pain is associated with a substantial negative impact on patients' quality of life. Persistent pain often interferes with sleep, physical functioning, mobility, work productivity, social interactions, and emotional well-being. Patients commonly experience anxiety, depression, fatigue, and cognitive impairment, which further contribute to disease burden and reduced health-related quality of life. The chronic nature of neuropathic pain frequently necessitates long-term treatment and ongoing medical care, resulting in significant healthcare utilization and economic costs. Epidemiological studies suggest that neuropathic pain affects approximately 6.9%-10% of the general population worldwide, although prevalence may vary according to diagnostic criteria, underlying etiology, and geographic region. Common causes include diabetic peripheral neuropathy, postherpetic neuralgia, radiculopathy, nerve compression syndromes, chemotherapy-induced peripheral neuropathy, traumatic nerve injury, and central nervous system disorders such as stroke and multiple sclerosis. With the increasing prevalence of diabetes, aging populations, and improved survival of patients with chronic neurological disorders, the burden of neuropathic pain is expected to rise further in the coming decades.⁵⁻⁷

Despite advances in the understanding of neuropathic pain pathophysiology, its management remains challenging. Current treatment guidelines recommend agents such as gabapentinoids (pregabalin and gabapentin), serotonin-norepinephrine reuptake inhibitors (duloxetine), tricyclic antidepressants, and topical therapies as first-line options.^{8,9} However, these therapies are frequently associated with incomplete pain relief, variable patient responses, dose-limiting adverse effects, and poor long-term adherence. Consequently, there is growing interest in adjunctive therapies that target additional mechanisms involved in the development and persistence of neuropathic pain.¹⁰

Increasing evidence suggests that neuroinflammation plays a critical role in the initiation and maintenance of neuropathic pain. Activation of mast cells, microglia, and astrocytes contributes to the release of pro-inflammatory mediators, leading to peripheral and central sensitization.^{11,12} Therefore, therapeutic strategies aimed at

modulating neuroinflammatory pathways may offer additional benefits in the management of neuropathic pain.

Palmitoylethanolamide (PEA) is an endogenous fatty acid amide belonging to the family of N-acyl ethanolamines and is recognized for its anti-inflammatory, neuroprotective, and analgesic properties. PEA exerts its effects through multiple mechanisms, including modulation of mast cell activation, regulation of glial cell activity, activation of peroxisome proliferator-activated receptor-alpha (PPAR- α), and reduction of neuroinflammatory signaling.^{13,14} These mechanisms have generated interest in the potential role of PEA as an adjunctive treatment option in neuropathic pain and other chronic pain conditions.

Clinical studies and systematic reviews have demonstrated that PEA may improve pain intensity, neuropathic symptoms, and functional outcomes while maintaining a favorable safety and tolerability profile. Furthermore, unlike many conventional neuropathic pain medications, PEA is generally well tolerated and is not associated with significant sedation, cognitive impairment, or dependence-related concerns, making it a potentially attractive option for long-term use.¹⁵⁻¹⁷

Although the scientific evidence supporting the efficacy and safety of PEA has expanded considerably, limited information is available regarding its real-world utilization, prescribing patterns, therapeutic positioning, and physician perceptions in routine clinical practice. Understanding how clinicians incorporate PEA-based formulations into treatment algorithms, the indications for which they are commonly prescribed, and their perceived effectiveness and tolerability can provide valuable insights into current practice patterns and help identify unmet clinical needs.

Therefore, the present cross-sectional survey was conducted to evaluate physicians' prescribing preferences, utilization patterns, perceived efficacy, safety, and clinical experience with PEA-based formulations in the management of neuropathic pain. The findings are expected to provide real-world evidence regarding the role of PEA-based therapy in contemporary neuropathic pain management and may help guide future clinical practice and research.

METHODS

This study was designed as a descriptive, questionnaire-based, cross-sectional survey conducted during the 70th Annual conference of the Indian orthopaedic association (IOACON 2025), held in Guwahati, Assam, India, from 15-20 December 2025. Orthopedic surgeons attending the conference who voluntarily agreed to participate and provided informed consent were included in the survey. Participation was entirely voluntary, and only responses from participants who consented to share their opinions were considered for analysis. A total of 93 orthopedic

surgeons completed the survey questionnaire, and their responses were included in the final analysis.

The survey instrument consisted of nine structured, multiple-choice questions developed to assess physicians' clinical perspectives and utilization patterns. The questionnaire was administered electronically using Google forms, and data was collected during the conference. Completed responses were exported to Microsoft excel for data compilation, cleaning, and management.

As the survey involved only healthcare professionals and did not include any patient participants, patient data, or patient interventions, an ethical waiver was obtained from an Independent Ethics Committee prior to study initiation. Data were analyzed using descriptive statistical methods, and the findings were summarized as frequencies and percentages to describe the distribution of participants' responses.

Ethical considerations

The study protocol was reviewed by an Independent Ethics Committee, and the study was granted an ethics committee waiver, as the survey was non-interventional, anonymized, and involved no patient data. Participation was entirely voluntary, and electronic informed consent was obtained from all respondents prior to survey initiation. Confidentiality and anonymity of participants were strictly maintained throughout the study.

RESULTS

The survey captured responses from 93 physicians regarding their clinical experience with PEA-based formulations. The results highlight prescribing practices, therapeutic positioning, perceived clinical effectiveness, safety, and factors influencing the adoption of PEA-based therapy in neuropathic pain management.

Table 1: Demographic details of participants.

Gender	Number of participants
Male	86
Female	7
Total	93
Age (mean±SD)	45.59±11.97

Demographic details

A total of 93 physicians participated in the survey assessing the clinical utilization and perceptions of PEA-based therapy in neuropathic pain management. The majority of respondents were male (86/93, 92.5%), while female physicians constituted 7.5% (7/93) of the study population. The mean age of the participants was 45.59±11.97 years (Table 1).

Prescribing frequency of PEA-based formulations

The frequency of prescribing PEA-based formulations in routine clinical practice is shown in figure 1. Most respondents reported regular use of PEA-based formulations, with nearly half (46/93,49.5%) indicating frequent use and 9.7% (9/93) reporting very frequent use. Occasional prescribing was reported by 24.7% (23/93) of physicians, whereas 9.7% (9/93) prescribed these formulations rarely. Only 5.4% (5/93) reported never prescribing PEA-based formulations.

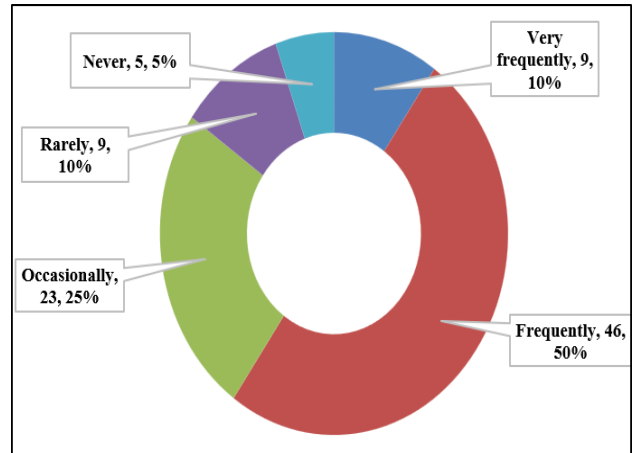


Figure 1: Prescribing frequency of PEA.

Clinical indications for PEA-based therapy

The clinical indications for which PEA-based formulations are prescribed are summarized in figure 2. Neuropathic pain was the most frequently reported indication, cited by 71.0% (66/93) of respondents. Chronic low back pain (60.2%;56/93) and peripheral nerve injury (57.0%;53/93) were also commonly reported indications. Use in fibromyalgia was relatively uncommon (3.2%;3/93). Five physicians (5.4%) reported not prescribing PEA-based formulations.

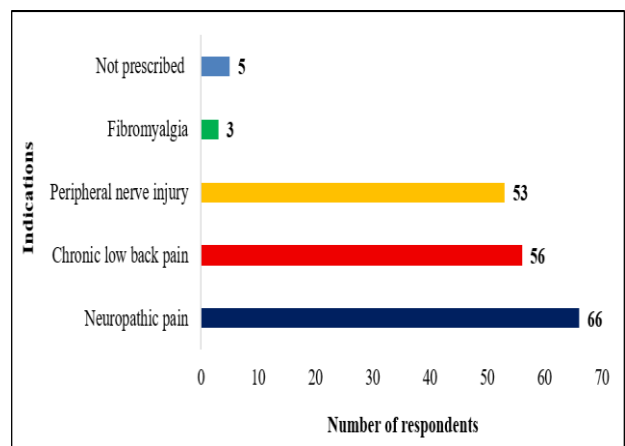


Figure 2: Physician-reported clinical indications for PEA-based therapy.

Timing of initiation of PEA-based therapy

Physicians' preferences regarding the stage of patient management at which PEA-based formulations are initiated are presented in figure 3. More than half of the respondents (56/93, 60.2%) reported initiating PEA-based therapy as an early adjunct to first-line treatment. Approximately one-quarter (25/93, 26.9%) preferred introducing PEA following an inadequate response to first-line agents such as pregabalin or gabapentin. A smaller proportion initiated therapy after inadequate response to antidepressants (3.2%; 3/93), while 7.5% (7/93) reserved PEA-based formulations for chronic or refractory neuropathic pain.

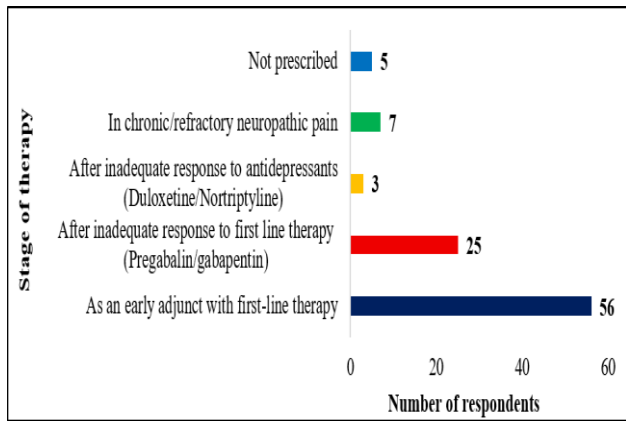


Figure 3: Timing of PEA-based therapy initiation in the management.

Perceived overall efficacy of PEA-based formulations

The perceived overall efficacy of PEA-based formulations in neuropathic pain management is illustrated in figure 4. Among all respondents, 24.7% (23/93) considered PEA-based therapy highly effective, whereas the majority (69.9%; 65/93) rated it as moderately effective. Notably, none of the respondents rated the therapy as minimally effective. Five physicians (5.4%) did not provide an efficacy assessment because they did not prescribe the formulation.

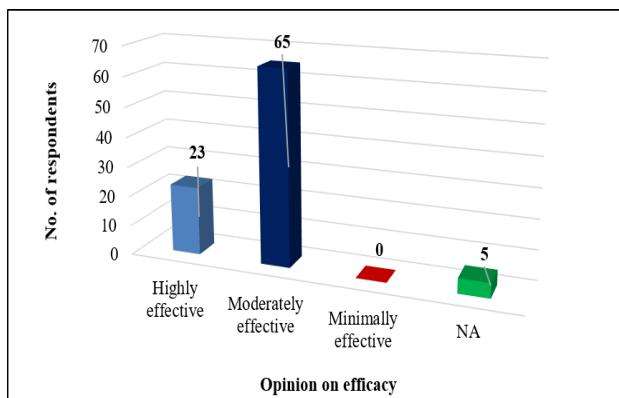


Figure 4: Perceived overall efficacy of PEA-based formulations.

Time to symptom improvement

Physicians' observations regarding the onset of symptom improvement following initiation of PEA-based therapy are shown in figure 5. Clinical improvement within 1-2 weeks was reported by 40.9% (38/93) of respondents, making it the most commonly observed timeframe. Improvement within 2-4 weeks was reported by 30.1% (28/93), while 23.7% (22/93) observed symptom improvement within 1-3 months.

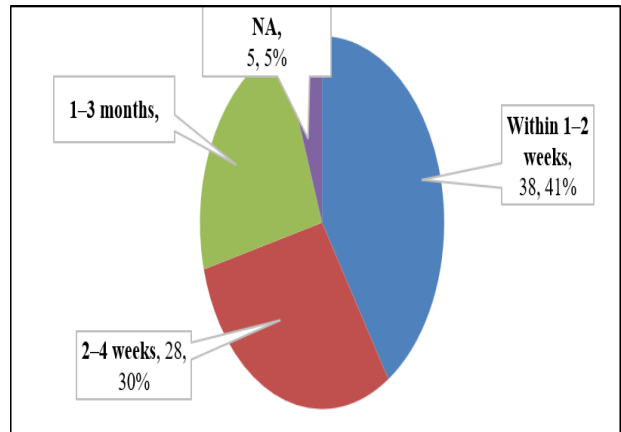


Figure 5: Onset of symptom improvement after initiation of PEA-based therapy.

Effectiveness in improving neuropathic symptoms

The perceived effectiveness of PEA-based formulations in improving key neuropathic symptoms, including pain, burning sensation, tingling, paresthesia, and sleep disturbance, is presented in figure 6. Approximately one-quarter of respondents (24.7%; 23/93) rated the therapy as highly effective, while the majority (69.9%; 65/93) considered it moderately effective. No respondent reported minimal effectiveness, indicating broad satisfaction with symptom control achieved using PEA-based therapy.

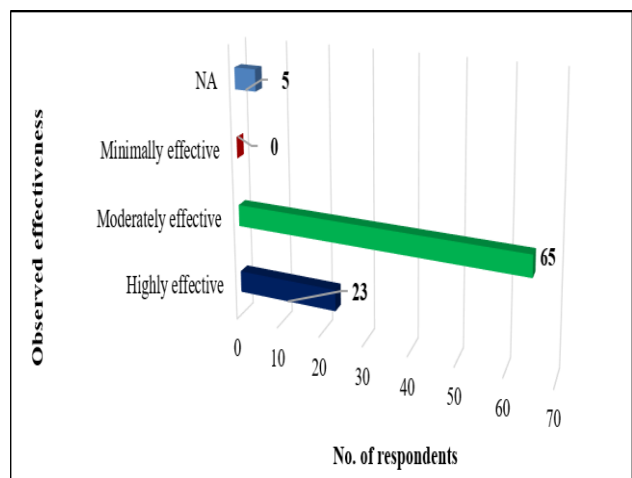


Figure 6: Physician assessment of the effectiveness of PEA-based formulations in neuropathic pain.

Safety and tolerability

Physicians’ assessment of the safety and tolerability profile of PEA-based formulations is shown in figure 7. The majority of respondents (83.9%; 78/93) described the formulation as very well tolerated with minimal side effects. Moderate safety concerns were reported by 9.7% (9/93) of physicians, while only one respondent (1.1%) reported significant safety concerns. These findings suggest a favorable safety and tolerability profile of PEA-based therapy in routine clinical practice.

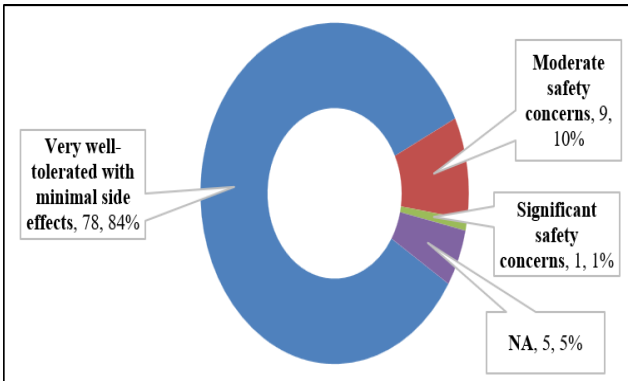


Figure 7: Perceived safety and tolerability profile of PEA-based formulations.

Factors influencing preference for PEA-based formulations

The factors influencing physicians’ preference for PEA-based formulations over other neuro-nutraceutical or combination products are summarized in figure 8. Once-daily dosing and improved patient compliance emerged as the most frequently cited factor (46.2%;43/93). Better tolerability compared with gabapentinoids such as pregabalin and gabapentin was reported by 33.3% (31/93) of respondents. Additionally, 15.1% (14/93) considered the presence of PEA 600 mg, along with its anti-inflammatory and neuroprotective properties, as a key determinant of their prescribing preference.

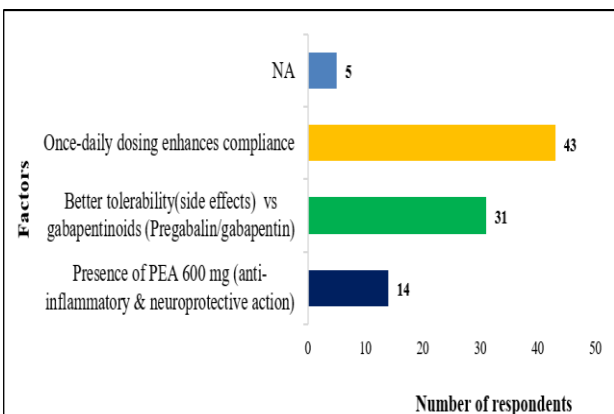


Figure 8: Key factors driving physician preference for PEA-based formulations.

Use of PEA-based formulations for long-term maintenance therapy

Physicians’ perspectives regarding the role of PEA-based formulations as long-term maintenance therapy for neuropathic pain are shown in figure 9. More than one-third of respondents (38.7%;36/93) reported routinely considering PEA-based formulations for long-term maintenance therapy, while a further 55.9% (52/93) indicated that they would prescribe them in selected patients. These findings suggest a high level of confidence among physicians regarding the long-term utility of PEA-based therapy in neuropathic pain management.

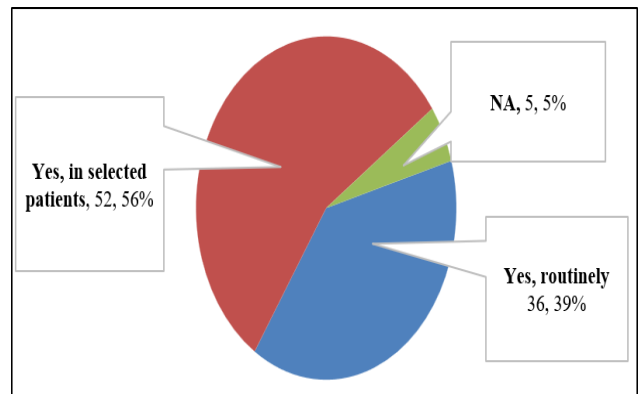


Figure 9: Physician opinions regarding long-term use of PEA-based formulations.

Overall, the survey demonstrated widespread utilization of PEA-based formulations in clinical practice, particularly for neuropathic pain, chronic low back pain, and peripheral nerve injury. As shown across figures 1-9, physicians reported favourable perceptions regarding efficacy, early symptom improvement, tolerability, and suitability for long-term management, supporting the role of PEA-based therapy as a valuable adjunctive option in the management of neuropathic pain.

DISCUSSION

The present cross-sectional survey provides valuable real-world insights into physicians’ utilization patterns, prescribing preferences, and clinical perceptions regarding PEA-based formulations in the management of neuropathic pain. The findings demonstrate widespread adoption of PEA-based therapy, with most respondents reporting frequent or occasional use, favourable perceptions of efficacy, good tolerability, and a willingness to incorporate PEA into long-term treatment strategies. These observations reflect the growing interest in multimodal approaches targeting both neuronal dysfunction and neuroinflammation in neuropathic pain management.

Neuropathic pain remains a significant therapeutic challenge despite the availability of established pharmacological options such as gabapentinoids,

antidepressants, and topical agents. Although these therapies are recommended as first-line treatments, their effectiveness is often limited by incomplete pain relief, adverse effects, and poor adherence during long-term treatment. Consequently, adjunctive therapies with complementary mechanisms of action have gained increasing attention. PEA, an endogenous lipid mediator with anti-inflammatory and neuroprotective properties, has emerged as a promising option in this regard. Previous mechanistic studies have demonstrated that PEA modulates mast cell activation, attenuates glial cell-mediated neuroinflammation, and activates PPAR- α signalling pathways, all of which are implicated in the pathogenesis of neuropathic pain.^{13,14,18}

A notable finding of the present survey was that nearly 60% of physicians reported initiating PEA-based therapy as an early adjunct to first-line treatment, whereas only a minority reserved its use for refractory disease. This observation suggests that many clinicians view PEA not merely as a rescue therapy but as a component of an integrated treatment strategy. Although current neuropathic pain guidelines do not universally position PEA among first-line pharmacological agents, accumulating clinical evidence has supported its use as an adjunctive treatment, particularly because of its favorable safety profile and potential to target neuroinflammatory mechanisms not adequately addressed by conventional therapies.^{8,2,16}

Neuropathic pain was the most commonly reported indication for PEA use in our survey, followed by chronic low back pain and peripheral nerve injury. These findings are consistent with published literature demonstrating potential benefits of PEA across various neuropathic and chronic pain conditions. A systematic review and meta-analysis by Lang-Ilievich et al, involving randomized controlled trials reported significant reductions in pain intensity among patients receiving PEA compared with control interventions.¹⁹ Similarly, Scuteri et al, concluded that available clinical evidence supports the analgesic effects of PEA across nociceptive, musculoskeletal, and neuropathic pain conditions.²⁰ Collectively, these findings support the broad spectrum of clinical indications reported by physicians in the present survey.

The perceived effectiveness of PEA-based formulations was highly favorable, with approximately 95% of respondents rating the therapy as either highly or moderately effective. Importantly, none of the respondents considered PEA minimally effective. Although physician perception does not substitute for objective clinical outcomes, these observations are consistent with published clinical studies demonstrating improvements in pain severity and neuropathic symptoms following PEA administration. A recent systematic review and meta-analysis found that PEA significantly reduced pain scores relative to comparators across diverse chronic pain conditions.²⁴ Similarly, pooled analyses and narrative reviews have reported clinically meaningful reductions in

pain intensity and symptom burden among patients receiving PEA-containing formulations.^{21-22,15}

The time to symptom improvement reported in our survey also aligns with existing literature. Approximately 41% of respondents observed clinical improvement within 1-2 weeks, while an additional 30% reported improvement within 2-4 weeks. Clinical studies evaluating PEA have similarly suggested that symptom improvement may occur within the first few weeks of treatment and continue to increase with prolonged administration. Extended-treatment analyses have demonstrated that pain reduction with micronized PEA may be time-dependent, with further improvements observed beyond the first month of therapy.²³ This may explain why a substantial proportion of physicians in the current survey considered PEA suitable for long-term maintenance therapy. An important finding of this survey was the favorable safety and tolerability profile attributed to PEA-based formulations. More than four-fifths of respondents considered the therapy very well tolerated, whereas only a small minority reported significant safety concerns. This perception is supported by published evidence indicating that PEA is generally associated with a low incidence of adverse events and excellent tolerability. Meta-analyses and systematic reviews have consistently highlighted the favorable safety profile of PEA, particularly when compared with therapies such as gabapentinoids, which are frequently associated with dizziness, somnolence, and cognitive adverse effects.¹⁹⁻²¹ The favorable tolerability profile likely contributed to the widespread acceptance of PEA as a long-term therapeutic option observed in this survey.

Interestingly, once-daily dosing and improved patient compliance emerged as the most frequently cited reasons for preferring PEA-based formulations. Treatment adherence is a critical determinant of outcomes in chronic pain management, and simplified dosing regimens have been shown to improve medication persistence and patient satisfaction. Although specific adherence data for PEA are limited, the preference for convenient dosing schedules observed in the present survey highlights an important practical consideration influencing real-world prescribing behaviour. The survey also demonstrated considerable physician confidence in the long-term use of PEA-based formulations, with nearly 95% of respondents indicating that they would routinely prescribe PEA or use it in selected patients as maintenance therapy. This finding is noteworthy because chronic neuropathic pain often requires prolonged treatment. Therapies that maintain effectiveness while minimizing adverse effects are therefore highly desirable. Published evidence suggests that PEA can be administered for extended periods with a favourable benefit-risk profile, supporting the perceptions expressed by physicians in this survey.^{24,25}

The findings of this study should be interpreted in light of certain limitations. First, the survey relied on physician-reported perceptions and experiences rather than objective

patient-level clinical outcomes. Second, the cross-sectional design precludes assessment of causal relationships between PEA use and clinical effectiveness. Third, responses may have been influenced by recall bias and individual prescribing preferences. Finally, the sample size, although adequate for exploratory analysis, may not fully represent prescribing practices across all healthcare settings and specialties. Despite these limitations, the study provides important real-world evidence regarding current clinical utilization of PEA-based formulations. The findings suggest that physicians perceive PEA as an effective, well-tolerated, and clinically useful adjunctive therapy for neuropathic pain and related conditions. Future prospective observational studies and large randomized controlled trials are warranted to further define the optimal positioning of PEA within neuropathic pain treatment algorithms and to validate the favorable clinical perceptions identified in this survey.

CONCLUSION

PEA-based formulations appear to be well integrated into contemporary clinical practice for the management of neuropathic pain, with physicians reporting favourable efficacy, excellent tolerability, and suitability for both early adjunctive use and long-term maintenance therapy. These findings underscore the growing clinical acceptance of PEA-based therapy as part of a multimodal approach targeting neuroinflammation in neuropathic pain. While the results reflect physician perceptions from real-world practice, further well-designed prospective studies are warranted to confirm their long-term clinical effectiveness and safety.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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