

Real-World Patterns of Cyclobenzaprine–Dexketoprofen Co-prescribing in Türkiye: A Nationwide Pharmacy Network-Based Study

Bulent GUMUSEL^{*}, Belma KOCER GUMUSEL^{**}

Real-World Patterns of Cyclobenzaprine–Dexketoprofen Co-prescribing in Türkiye: A Nationwide Pharmacy Network-Based Study

Türkiye’de Siklobenzaprin-Deksetopropfen Birlikte Reçete Edilmesinin Gerçek Dünya Modeli: Ulusal Eczane Bazlı Çalışma

SUMMARY

Pharmacologic management of acute musculoskeletal (MSK) pain with muscle spasm frequently involves the combination of nonsteroidal anti-inflammatory drugs (NSAIDs) and skeletal muscle relaxants (SMRs). While the combination of cyclobenzaprine and various NSAIDs has been studied, the co-prescribing of cyclobenzaprine with dexketoprofen—a widely used NSAID in Türkiye—lacks specific evaluation. This study aims to quantify the prevalence and characterize the patterns of cyclobenzaprine–dexketoprofen co-prescribing in routine outpatient practice in Türkiye. A retrospective, cross-sectional drug utilization study was conducted using dispensing-linked prescription data from a network of 3,864 community pharmacies across Türkiye between January 1, 2022, and December 31, 2024. Prescriptions containing cyclobenzaprine were identified and analyzed for concurrent NSAID dispensing. The primary outcomes were the proportion of cyclobenzaprine prescriptions containing an NSAID and the specific prevalence of dexketoprofen co-prescribing. The study dataset included more than 200 million outpatient prescriptions dispensed through an average of 3,864 community pharmacies per year across Türkiye (January 1, 2022–December 31, 2024). Oral solid NSAIDs (ATC M01A) accounted for 19% of all prescriptions, while oral solid skeletal muscle relaxants (ATC M03B) accounted for 6%. Within the oral solid M03B market, 43% were monotherapy products and 57% were fixed-dose combinations; among combinations, 65% contained an NSAID and 35% contained paracetamol. Among all cyclobenzaprine prescriptions, 52% were co-dispensed with a monotherapy oral solid NSAID, and 13% were co-dispensed specifically with oral solid dexketoprofen (corresponding to approximately one-quarter of cyclobenzaprine prescriptions with an NSAID co-dispensing). The co-prescribing of cyclobenzaprine and dexketoprofen is a common clinical practice in Türkiye, representing a significant portion of acute pain with muscle spasm management strategies. This pattern reflects a pragmatic clinical approach targeting both nociceptive and spasmodic components of MSK pain. Given the absence of randomized controlled trials specifically evaluating this combination, these real-world findings highlight a priority area for future comparative effectiveness and safety research.

Keywords: Nonsteroidal anti-inflammatory drugs, cyclobenzaprine, dexketoprofen, acute musculoskeletal pain, real-world data

ÖZ

Akut kas-iskelet (MSK) ağrısının ve kas spazmının farmakolojik tedavisi sıklıkla nonsteroid antiinflamatuar ilaçlar (NSAİ’ler) ve iskelet kası gevşeticilerinin (SMR’ler) kombinasyonunu içerir. Siklobenzaprin ve çeşitli NSAİ’lerin kombinasyonu incelenmiş olsa da, Türkiye’de yaygın olarak kullanılan bir NSAİ olan deksketopropfen ile siklobenzaprinin birlikte reçete edilmesi konusunda spesifik bir değerlendirme eksikliği bulunmaktadır. Bu çalışma, Türkiye’deki rutin poliklinik uygulamalarında siklobenzaprin-deksketopropfen birlikte reçete edilmesinin yaygınlığını belirlemeyi ve karakterize etmeyi amaçlamaktadır. 1 Ocak 2022 ile 31 Aralık 2024 tarihleri arasında Türkiye genelindeki 3864 eczaneden oluşan bir ağdan elde edilen reçete verileri kullanılarak retrospektif, kesitsel bir ilaç kullanım çalışması yapılmıştır. Siklobenzaprin içeren reçeteler belirlenmiş ve eş zamanlı NSAİ reçetesi açısından analiz edilmiştir. Birincil sonuçlar, NSAİ içeren siklobenzaprin reçetelerinin oranı ve deksketopropfenin birlikte reçete edilme sıklığıdır. Çalışma veri seti, Türkiye genelinde yılda ortalama 3864 eczane aracılığıyla dağıtılan 200 milyondan fazla ayakta tedavi reçetesini içermiştir (1 Ocak 2022 – 31 Aralık 2024). Oral solid NSAİ’ler (ATC M01A) tüm reçetelerin %19’unu, oral solid iskelet kası gevşeticileri (ATC M03B) ise %6’sını oluşturmıştır. Oral solid M03B pazarı içinde, %43 monoterapi ürünleri ve %57 sabit doz kombinasyonları yer almaktadır; kombinasyonlar arasında %65 NSAİ ve %35 parasetamol bulunmaktadır. Tüm siklobenzaprin reçetelerinin %52’si tek başına kullanılan oral solid NSAİ’lerle birlikte, %13’ü ise özellikle oral solid deksketopropfen ile birlikte reçete edilmiştir (bu da NSAİ ile birlikte reçete edilen siklobenzaprin reçetelerinin yaklaşık dörtte birine karşılık gelmektedir). Siklobenzaprin ve deksketopropfenin birlikte reçete edilmesi Türkiye’de yaygın bir klinik uygulamadır ve kas spazmı yönetimi stratejileriyle birlikte akut ağrının önemli bir bölümünü temsil etmektedir. Bu durum, kas-iskelet sistemi ağrısının hem nosiseptif hem de spazmodik bileşenlerini hedefleyen pragmatik bir klinik yaklaşımı yansıtmaktadır. Bu kombinasyonu özel olarak değerlendiren randomize kontrollü çalışmaların yokluğu göz önüne alındığında, bu gerçek yaşam verileri, gelecekteki karşılaştırmalı etkililik ve güvenlik araştırmaları için öncelikli bir alanı vurgulamaktadır.

Anahtar Kelimeler: Steroid olmayan antiinflamatuar ilaçlar, siklobenzaprin, deksketopropfen, akut kas-iskelet ağrısı, gerçek yaşam verisi

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^{*} ORCID: 0000-0002-7533-7949, Department of Pharmacology, Faculty of Pharmacy, Istanbul Okan University, Istanbul, Türkiye

^{**} ORCID: 0000-0003-4311-2291, Department of Toxicology, Faculty of Pharmacy, Istanbul Okan University, Istanbul, Türkiye

INTRODUCTION

Pain is the most frequently reported symptom in the general population and across routine clinical care (Kroenke, 2003). In the United States alone, pain accounts for more than 100 million outpatient encounters annually and imposes an economic burden exceeding 100 billion USD when direct healthcare costs and productivity losses are considered (Stewart, Ricci, Chee, Morganstein, & Lipton, 2003). As a major public health challenge, pain has prompted global initiatives, including a World Health Organization campaign, and is often framed clinically as the “fifth vital sign.” Despite advances in diagnosis and treatment, pain remains a leading cause of both temporary and permanent disability worldwide (Breivik, 2002; Kroenke, Krebs, & Bair, 2009). Recent Global Burden of Disease analyses show that musculoskeletal disorders (MSDs) remain among the leading causes of disability worldwide, and their burden is projected to increase substantially in the coming decades (Gill et al., 2023). In 2021, there are projected to be 1.686 billion cases of musculoskeletal disorders (MSDs) worldwide, an increase of 95% since 1990. Global MSD mortality is decreasing at a rate of 0.265% per year. The number of MSD cases is projected to increase to 2.161 billion by 2035 (Liu et al., 2025).

Acute musculoskeletal (MSK) spasm represents a common and typically self-limiting clinical presentation, characterized by localized pain, muscle tenderness, stiffness, and reduced range of motion. The natural history is generally favorable, with approximately 60% of cases resolving within one week and nearly 90% within six weeks, regardless of intervention. Nevertheless, shortening this recovery window is clinically meaningful, as effective symptom control may reduce functional impairment, limit work absenteeism, and prevent progression to chronic pain states. Consequently, pharmacologic management frequently includes nonsteroidal anti-inflammatory drugs (NSAIDs) and skeletal muscle relaxants (SMRs), either as monotherapy or in combination

(Kinkade, 2007; Pengel, Herbert, Maher, & Refshauge, 2003; Qaseem et al., 2017).

Pain and muscle spasm are often described as components of a self-perpetuating “pain–spasm–pain” cycle. Nociceptive stimuli arising from musculoskeletal injury may trigger reflex muscle contraction as a protective mechanism (Kane, 1964). Sustained muscle contraction can subsequently reduce local blood flow, increase metabolic by-products, and enhance nociceptor sensitization, thereby amplifying pain perception. Clinical observations in low back pain have questioned the consistency of measurable spasm, yet the functional interplay between pain and reflex muscle activity remains widely recognized (Roland, 1986). Contemporary perspectives emphasize that interruption of this cycle may be a therapeutic target in acute musculoskeletal conditions (Budhyanti & Panjaitan, 2018). Contemporary evidence highlights the role of central sensitization, whereby repeated nociceptive input enhances the responsiveness of central neurons, amplifying pain perception and sustaining musculoskeletal pain states (Curatolo, 2024).

Acute low back pain—the prototypical acute MSK disorder—has been extensively studied as a model condition. High-quality evidence demonstrates that acetaminophen offers no clinically meaningful benefit over placebo, whereas NSAIDs provide modest but statistically significant overall improvement, with an absolute benefit of approximately one additional responder for every 11 patients treated (Borenstein & Korn, 2003). Contemporary clinical guidelines therefore recommend NSAIDs as first-line pharmacologic therapy and endorse short-term use of SMRs in selected patients, particularly when painful muscle spasm accompanies inflammation. These recommendations implicitly support combination strategies targeting complementary pain mechanisms (Qaseem et al., 2017).

Cyclobenzaprine hydrochloride, introduced in 1977, is indicated as an adjunct to rest and physical therapy for the relief of muscle spasm associated with

acute, painful MSK conditions. Cyclobenzaprine is structurally similar to tricyclic antidepressants but differs from amitriptyline by the presence of an additional double bond in its central ring structure, which contributes to distinct pharmacological properties (Cimolai, 2009). Structurally related to tricyclic antidepressants, cyclobenzaprine exerts its effect centrally, reducing tonic somatic motor activity and alleviating spasm without direct action on skeletal muscle. Controlled clinical trials and extensive post-marketing experience demonstrate improvements in muscle spasm, local pain and tenderness, and range of motion, with a generally favorable safety profile and few serious adverse events. Importantly, a dose of 5 mg three times daily is as effective as 10 mg three times daily while producing fewer anticholinergic and sedative adverse effects. Unlike some alternative SMRs, such as carisoprodol, cyclobenzaprine has not been associated with dependence or withdrawal phenomena following discontinuation, even after longer use (Browning, Jackson, & O'Malley, 2001). Dexketoprofen, the pharmacologically active S(+)-enantiomer of ketoprofen, is a potent NSAID with analgesic, anti-inflammatory, and antipyretic properties. By selectively administering the active enantiomer, dexketoprofen achieves effective pain relief at lower doses than racemic ketoprofen, with a rapid onset of action that makes it particularly attractive for acute pain management. These pharmacodynamic characteristics have supported its widespread use in various acute pain settings, including MSK conditions (Kuczyńska, Pawlak, & Nieradko-Iwanicka, 2022).

From a mechanistic perspective, the combination of an NSAID and an SMR is biologically plausible, as inflammation-driven nociception and reflex muscle spasm frequently coexist in acute MSK disorders. Cyclobenzaprine has been evaluated in combination with NSAIDs such as ibuprofen and naproxen, with mixed but generally supportive evidence for additive symptom relief in selected patients. However, despite the common use of dexketoprofen in routine clinical practice—particularly in certain regions—no ran-

domized controlled trial has evaluated the combination of cyclobenzaprine with dexketoprofen (Hanna & Moon, 2019; Patel et al., 2019).

Despite the widespread clinical use of NSAID–SMR combinations, evidence for specific agent pairings remains limited. Cyclobenzaprine has been evaluated in combination with NSAIDs such as ibuprofen and naproxen; however, no randomized controlled trials have examined its use alongside dexketoprofen, despite the frequent use of both agents in routine practice. In the absence of trial data, real-world prescribing patterns offer an important opportunity to characterize current clinical behavior. This study was designed as a cross-sectional analysis using real-world prescription data, enabling evaluation of an *a priori* hypothesis derived from routine clinical observations that cyclobenzaprine and dexketoprofen—both reimbursed and widely used in Türkiye—are frequently co-prescribed in outpatient practice. The objective of this study was therefore to quantify the prevalence and characterize the patterns of cyclobenzaprine–dexketoprofen co-prescribing in routine outpatient care.

MATERIALS AND METHODS

Study design and data source

We conducted a retrospective, cross-sectional drug utilization analysis using dispensing-linked prescription data obtained from community pharmacies in Türkiye. The dataset comprised prescriptions recorded between January 1, 2022, and December 31, 2024, captured from an average panel of 3,864 community pharmacies per year [Data provided by Vademecum]. Prescriptions were linked to dispensing events, allowing characterization of medications actually supplied to patients rather than those solely prescribed.

The source network comprises community pharmacies distributed across all seven geographical regions of Türkiye and captures approximately 20% of all outpatient prescriptions nationally during 2022–2024. The regional distribution of contributing

pharmacies mirrors the national pharmacy footprint, supporting geographic representativeness of the sample and the generalizability of prescribing patterns reported herein.

All data were provided in a de-identified, aggregated form. No patient-level identifiers, longitudinal follow-up, or clinical outcome data were available or accessed for this analysis.

All analyses were conducted at the prescription level. As patient-level identifiers were not available in the dataset, it was not possible to link prescriptions to individual patients or to account for repeated prescriptions issued to the same individual.

Study population and prescription identification

The analytic frame included all outpatient prescriptions containing cyclobenzaprine during the study period. Prescriptions were identified based on active ingredient and pharmaceutical formulation. For the primary analysis, cyclobenzaprine-containing prescriptions were evaluated irrespective of dose strength or treatment duration.

Co-prescribing was defined at the prescription level as the presence of cyclobenzaprine and at least one additional medication dispensed within the same prescription record. NSAIDs were identified using Anatomical Therapeutic Chemical (ATC) classification codes, and individual agents were further classified by active ingredient. Dexketoprofen was pre-specified as the primary NSAID of interest.

Outcomes and endpoints

The primary endpoints were:

1. The proportion of cyclobenzaprine-containing prescriptions that included at least one NSAID, and
2. The proportion of cyclobenzaprine-containing prescriptions that included dexketoprofen.

Secondary descriptive endpoints included the proportion of dexketoprofen among all NSAIDs

co-prescribed with cyclobenzaprine.

To contextualize co-prescribing patterns, a class-level benchmarking analysis was performed. This analysis examined co-dispensing patterns of oral solid skeletal muscle relaxant monotherapy with oral solid NSAID monotherapy, enabling comparison of cyclobenzaprine–dexketoprofen use with broader SMR–NSAID prescribing behavior.

Statistical analysis

All analyses were descriptive in nature. Results are reported as counts and proportions. No inferential statistical testing, hypothesis testing, or modeling was performed, consistent with the study's objective to characterize real-world prescribing patterns rather than assess causal associations or comparative effectiveness.

Data management and analyses were conducted using standard analytical software. Given the use of aggregated, de-identified data, no adjustments for patient-level clustering or repeated observations were applied.

Ethical considerations

This study used fully de-identified, aggregated prescription data and did not involve direct patient contact or access to individual-level clinical information. In accordance with local regulations and the Declaration of Helsinki, studies using fully anonymized, aggregated secondary data are exempt from formal ethical committee approval, and informed consent was not required. In accordance with national regulations and the Declaration of Helsinki, studies using fully anonymized, aggregated secondary data are exempt from formal ethics committee approval.

RESULTS

Pharmacy distribution (and geographic representativeness)

This study is based on a nationwide community-pharmacy network that captures dispensing-linked outpatient prescription data across all seven geographical regions of Türkiye, supporting geographic

representativeness of the sample. Consistent with this, the sample is described as covering approximately 20% of all prescriptions written in Türkiye during the study period and as being derived from a broad pharmacy network rather than a regional/local subset (Table 1.).

Table 1. Regional distribution of pharmacies in Türkiye vs contributing sample pharmacies (%)

Region	National pharmacies	Sample pharmacies	Sample prescription coverage
Mediterranean	14	6	5
Eastern Anatolia	5	3	3
Aegean	15	13	15
Southeastern Anatolia	9	4	3
Central Anatolia	17	17	16
Black Sea	9	12	12
Marmara	31	18	21

Total number of prescriptions in the sample (overall universe)

The dataset comprised dispensing-linked outpatient prescriptions recorded between January 1, 2022, and December 31, 2024, captured from an average

panel of 3,864 community pharmacies per year. The manuscript describes the analytic dataset as encompassing more than 200 million prescriptions, providing a large national frame for estimating real-world prescribing patterns (Table 2.).

Table 2. Total number of prescriptions and number of pharmacies

Years	Number of Pharmacies	Number of prescriptions
2022	3,911	71,872,062
2023	3,831	75,421,475
2024	3,851	61,264,156
Total/Mean	3,864	209,557,693

Total oral solid NSAIDs (ATC M01A) and total oral solid skeletal muscle relaxants (ATC M03B)

Across 2022–2024, 19% (n=40,655,201) of all prescriptions in the sample contained oral solid NSAIDs classified under ATC M01A. In the same period, 6% (n=12,437,547) of all prescriptions in the sample contained oral solid skeletal muscle relaxants classified under ATC M03B.

In the oral-solid skeletal muscle relaxant (SMR) prescription cohort (n=12,437,547), 2,619,420 prescriptions included an NSAID as a separate medi-

cation, and 4,703,917 included an NSAID within a fixed-dose combination (FDC). Overall, 7,323,337 SMR prescriptions contained an NSAID in either form (59%).

Oral solid monotherapy vs fixed-dose combination muscle relaxants within the M03B market

Within oral solid M03B prescriptions, 43% were monotherapy products, whereas 57% were fixed-dose combination (FDC) formulations. Among M03B fixed-dose combinations, 35% contained paracetamol, while 65% contained an NSAID (Table 3.).

Table 3. Composition of M03B fixed-dose combinations (paracetamol-containing vs NSAID-containing)

Years	2022	2023	2024	Total
Paracetamol-containing	806,601	886,806	787,350	2,484,767
NSAID-containing	1,414,211	1,723,649	1,566,057	4,703,917
Total	2,222,822	2,612,455	2,353,407	7,188,684

Among prescriptions containing monotherapy oral solid muscle relaxants, the proportion that also included a monotherapy oral solid NSAID was 49%.

Co-prescribing of cyclobenzaprine with monotherapy oral solid NSAIDs and with oral solid dextropropofol

Among all cyclobenzaprine prescriptions, the

proportion co-prescribed with a monotherapy oral solid NSAID was 52%. Among all cyclobenzaprine prescriptions, the proportion co-prescribed with oral solid dextropropofol was 13% (Table 4.).

In total, 824,826 cyclobenzaprine prescriptions were identified; 425,356 included an NSAID (52%). Among cyclobenzaprine prescriptions with an NSAID, 106,115 included dextropropofol (25%).

Table 4. Co-prescribing of cyclobenzaprine with monotherapy oral solid NSAIDs and with oral solid dextropropofol

Years	2022	2023	2024	Total
Mono oral solid NSAID-containing	90,433	159,540	175,383	425,356
Dextropropofol-containing	26,501	39,421	40,193	106,115
Total number of cyclobenzaprine prescriptions	188,539	302,312	333,975	824,826

DISCUSSION

In this large, national analysis of community pharmacy dispensing data in Türkiye, approximately half of cyclobenzaprine prescriptions were co-dispensed with a monotherapy oral solid NSAID (52%), and 13% included dextropropofol; dextropropofol represented approximately one-quarter of NSAIDs co-dispensed with cyclobenzaprine. Together, these findings indicate that combination therapy with a skeletal muscle relaxant and an NSAID—particularly dextropropofol—is a common and well-established practice in routine outpatient care.

When interpreted in an international context, the co-prescribing patterns observed in this study appear broadly consistent with existing literature on the management of acute musculoskeletal pain. In a study of data collected between 2002 and 2006, physicians commonly prescribed NSAIDs, muscle relaxants, and opioids in combination. In this study, 26% of patients received an NSAID in combination with a muscle relaxant, and another 26% received an NSAID in combination with an opioid (Friedman, Chilstrom, Bijur, & Gallagher, 2010). In another study, the use of NSAIDs/acetaminophen was 37% in 1999-2000 and 25% in 2009-2010. In contrast, the use of narcotics was 19% and 29% during the same time peri-

od (Mafi, McCarthy, Davis, & Landon, 2013). In this context, the proportion of cyclobenzaprine prescriptions co-dispensed with NSAIDs in our study (52%) aligns with these international observations. However, the relatively high representation of dextropropofol among NSAIDs likely reflects region-specific factors, including local prescribing practices, drug availability, and reimbursement policies within the Turkish healthcare system. These findings highlight both the global consistency of combination therapy approaches and the importance of local context in shaping specific drug utilization patterns.

These prescribing patterns are consistent with contemporary clinical approaches to acute musculoskeletal pain, in which pharmacologic strategies often aim to address both inflammatory and neuromuscular contributors to symptoms. In real-world settings, clinicians frequently pair a rapid-acting NSAID with a centrally acting antispasmodic to achieve early pain relief, reduce muscle spasm, and facilitate return of function. The prominence of dextropropofol among NSAID co-prescriptions likely reflects its pharmacologic profile, including rapid onset of analgesia and high potency at relatively low doses, which may be perceived as advantageous in acute pain presentations (Qaseem et al., 2017).

From a mechanistic perspective, the co-use of cyclobenzaprine and dextetoprofen is biologically plausible. Dextetoprofen exerts potent inhibition of cyclo-oxygenase pathways that mediate peripheral inflammation and nociception, while cyclobenzaprine acts centrally to reduce tonic somatic motor activity and muscle spasm. Acute musculoskeletal pain is frequently conceptualized within a “pain-spasm-pain” cycle, in which nociceptive input triggers reflex muscle contraction as a protective response (Kane, 1964) that may further exacerbate pain through ischemia and sustained motor activity (Budhyanti & Panjaitan, 2018). Although the consistency of objectively measurable muscle spasm has been debated in clinical settings such as low back pain (Roland, 1986), the functional interplay between pain and reflex muscle activity remains widely recognized. The most frequently associated diagnoses in this study—dorsalgia, myalgia, and other soft tissue disorders—are conditions in which both inflammation and reflex muscle spasm are prominent contributors to pain and functional limitation. In such contexts, combination therapy may theoretically interrupt different components of this cycle and thereby provide faster symptom relief and functional improvement than either agent alone (Hanna & Moon, 2019).

Safety considerations remain central to the interpretation of these findings. Cyclobenzaprine is associated with dose-dependent sedation and anticholinergic effects, which warrant particular caution in older adults and in patients with hepatic impairment, where dose reduction or avoidance is recommended in moderate to severe dysfunction. Dextetoprofen, like other NSAIDs, carries well-established risks of gastrointestinal bleeding, renal impairment, and cardiovascular events, especially with prolonged use or in high-risk populations. These risks underscore the importance of careful patient selection, short treatment durations, and consideration of gastroprotective strategies when NSAIDs are used (Joo et al., 2020; Kanno & Moayyedi, 2020). In combination, clinically relevant concerns include cumulative anticholinergic exposure in older

adults, additive CNS depression, and combined renal toxicity risk. The observed co-prescribing patterns, therefore, highlight the need to ensure that combination therapy remains targeted, time-limited, and aligned with guideline recommendations.

These findings should also be interpreted in the context of the Turkish outpatient analgesic market, where combination-based approaches appear common. In our dataset, fixed-dose combination products account for a substantial share of the oral solid M03B market and most combinations contain an NSAID, which may normalize concomitant SMR-NSAID use in routine practice. In addition, regional availability, reimbursement dynamics, and local prescribing habits could contribute to the prominence of dextetoprofen among NSAID co-dispensing patterns.

There was a ~77% increase in cyclobenzaprine prescriptions between 2022 and 2024 (188,539 to 333,975). This trend is possibly related to regulatory changes, new product launches, or changes in prescribing practices. But the drivers are mostly unknown from the prescription data alone.

This study has several notable strengths. The use of a very large national dataset encompassing more than 200 million prescriptions provides robust estimates of real-world prescribing patterns and enhances the generalizability of the findings within Türkiye. The contemporary study period (2022–2024) further strengthens the relevance of the results to current clinical practice. However, several limitations should be acknowledged. First, the descriptive, cross-sectional design precludes inference regarding clinical appropriateness, effectiveness, or safety of the observed combinations. Second, the absence of patient-level data limited our ability to assess dosing, treatment duration, repeat prescribing, or clinical outcomes, including symptom resolution or adverse events. Third, as analyses were performed at the prescription level and patient-level identifiers were not available, repeated prescriptions for the same individual could not be identified. This may have led to an overesti-

mation of prescribing frequencies and limits interpretation at the patient level. Fourth, the absence of diagnostic information in the dataset limits the ability to directly link prescribing patterns to specific clinical indications. Finally, co-dispensing within a single prescription does not necessarily confirm concurrent use over time, particularly in the absence of information on prescribed duration or adherence.

Future research should build on these findings in several ways. Incorporating dose, strength, and duration data would allow evaluation of adherence to recommended short-course use and enable dose-response analyses. Linkage to patient-level outcomes—such as repeat healthcare visits, functional recovery, opioid rescue therapy, and adverse events including gastrointestinal bleeding or central nervous system effects—would provide critical insight into the clinical impact of this co-prescribing pattern. Additional analyses examining regional variation, prescriber specialty, and practice setting, using cluster-robust or multilevel methods, could further elucidate drivers of combination therapy. Sensitivity analyses that vary co-dispensing windows and exclude complex multi-analgesic regimens would also help assess the robustness of the observed patterns.

CONCLUSION

In conclusion, co-prescribing of cyclobenzaprine and dextetoprofen is common in routine outpatient practice in Türkiye and appears to reflect a pragmatic approach to managing acute musculoskeletal pain. This interpretation is supported by our prescription analysis, which demonstrated that NSAIDs were present in approximately 59% of skeletal muscle relaxant prescriptions and that more than half of cyclobenzaprine prescriptions were issued in combination with an NSAID. While mechanistically plausible and aligned with common clinical reasoning, the appropriateness and outcomes of this combination cannot be determined from prescribing data alone. Further outcome-oriented and longitudinal studies are needed to distinguish targeted, short-term combination

use from habitual prescribing and to inform evidence-based optimization of acute pain management.

AUTHOR CONTRIBUTION STATEMENT

The conceptualization, methodology, investigation, data curation, formal analysis, visualization, writing – original draft, writing – review & editing, project administration (BG, BKG).

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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