New Tools, Same Goal: Fast Acute Pain Control With Fewer Opioids

Bill McCarberg, MD

doi:10.12788/fp.0790

Sponsorship: This activity is sponsored by Primary Care Education Consortium and is funded by an educational grant from Vertex Pharmaceuticals.

CONTINUING MEDICAL EDUCATION

LEARNING OBJECTIVES

At the end of the activity, participants will be able to:

- **Integrate** emerging nonopioid therapies, including selective $Na_v1.8$ inhibitors, into individualized, opioid-sparing treatment regimens for common acute pain presentations in primary care.
- **Understand** the role of voltage-gated sodium channels in C-fiber nociceptors for transmitting pain signals from the peripheral nervous system to the central nervous system.
- **Apply** newer acute pain treatments for eligible patients to maximize effectiveness and minimize adverse events.

TARGET AUDIENCE

Family physicians and clinicians who wish to gain increased knowledge and greater competency regarding primary care management of acute pain.

FACULTY

Bill McCarberg, MD (retired)
Former Director of Pain Management
Kaiser Permanente
San Diego, CA
President
Western Pain Society and American Academy of Pain Medicine

ACKNOWLEDGMENT

Editorial support was provided by Ellen Feldman, MD, at Primary Care Education Consortium.

DISCLOSURES

As a continuing medical education provider holding Joint Accreditation, Primary Care Education Consortium (PCEC) requires any individual in a position to influence educational content to disclose any financial interest or other personal relationship with any commercial interest. This includes any entity producing, marketing, re-selling, or distributing health care goods or services consumed by, or used on, patients. Mechanisms are in place to identify and mitigate any potential conflict of interest prior to the start of the activity. All relevant financial relationships have been mitigated. In addition, any discussion of off-label, experimental, or investigational use of drugs or devices will be disclosed by the faculty.

Dr. McCarberg has no disclosures to report.
Dr. Feldman has no disclosures to report.

ACCREDITATION

In support of improving patient care, PCEC is jointly accredited by the Accreditation Council for Continuing Medical Education (ACCME), the Accreditation Council for Pharmacy Education (ACPE), the American Academy of PAs (AAPA), and the American Nurses Credentialing Center (ANCC) to provide continuing education for the health care team. CME/CE credit is available from October 1, 2026, to March 31, 2027.

CREDIT DESIGNATION

This activity was planned by and for the health care team, and learners will receive 1.0 CME/CE credits (type dependent upon designation). Learners may select 1.0 *AMA PRA Category 1 Credits*™, 1.0 ANCC contact hours or 1.0 AAPA Category 1 CME credits, or a certificate of participation.

CME/CE credit is available from October 1, 2026, to March 31, 2027.

To receive credit: visit https://www.pceconsortium.org/survey/post/acutepain

INTRODUCTION

Pain remains one of the most common and challenging reasons patients seek care, accounting for an estimated 30% to 40% of all primary care visits.[1,2] Despite a shared goal of balancing pain relief, functional improvement, and minimal adverse medication effects, pain management often is frustrating for patients and clinicians alike.[2] Many clinicians have learned a bitter lesson from the opioid era: well-intentioned efforts to relieve suffering, when not grounded in careful risk assessment and clear treatment goals, can lead to unintended harm at both the individual and population levels.

Analgesics, key in acute pain treatment, are mainly divided into opioids and nonopioids.[3] Opioids, used for moderate to severe pain, bind to receptors in the brain and spinal cord to inhibit pain transmission and boost descending inhibition.[3,4] Nonopioid options for milder acute pain include acetaminophen, nonsteroidal anti-inflammatory drugs (NSAIDs), and topical agents such as lidocaine, topical diclofenac, and capsaicin or counterirritants such

Key takeaways

- Customize the analgesic choice to each patient, considering comorbidities and individual risk factors.
- Start with optimized nonopioid multimodal care and prescribe opioids (immediate-release, low-dose, and time-limited) only if the benefits will outweigh risks to the patient.
- $Na_V1.8$ inhibitors expand opioid-sparing options by targeting peripheral nociceptive signaling.
- Base pharmacologic and nonpharmacologic treatment on function, not a pain score.
- With an understanding of how $Na_V1.8$ channels in peripheral C-fibers transmit pain signals, clinicians can better explain the rationale for targeted therapy to patients and support adherence.

as menthol, methyl salicylate, and camphor when pain is localized. NSAIDs inhibit cyclooxygenase enzymes, reducing prostaglandin-mediated inflammation and peripheral sensitization. Acetaminophen has a less fully defined mechanism but appears to act primarily within the central nervous system, possibly through inhibition of central prostaglandin synthesis and modulation of descending serotonergic pain pathways, with minimal peripheral anti-inflammatory activity.[3,5]

Primary care clinicians (PCC) face a dilemma: opioids are effective but carry risks, including misuse, sedation, respiratory depression, and dependence, along with regulatory scrutiny. Nonopioid options are limited by ceiling effects, incomplete pain relief, or patient contraindications like renal, gastrointestinal, or cardiovascular issues. This creates a narrow window where clinicians must balance undertreating pain against the harms of potent therapies, often lacking clear intermediate options.[2-5]

WHAT IS NEXT?

The acute pain toolkit is evolving. In January 2025, the US Food and Drug Administration (FDA) approved suzetrigine, the first nonopioid analgesic for moderate-to-severe acute pain in adults.[6] This, along with the 2022 Centers for Disease Control and Prevention (CDC) guidelines' focus on nonopioid strategies and reassessment, offers clinicians a new option and an updated framework.[7]

Suzetrigine provides pain relief by selectively inhibiting the $Na_V1.8$ sodium channel in peripheral neurons that transmits pain signals to the central nervous system (CNS). This mechanism avoids CNS side effects like respiratory depression and the addiction risks associated with opioids.[6,8]

BOX 1. From poppy to periphery: a historical perspective

Historically, pain management has relied heavily on 2 approaches: opioids and anti-inflammatory agents, supplemented by acetaminophen.[9] Suzetrigine represents a new mechanism—a selective $Na_V1.8$ inhibitor that blocks pain signals in peripheral C-fiber nociceptors without impacting the brain. It delivers efficacy comparable to opioid combinations while avoiding many of the limitations that have long constrained pain management.[1]

ACUTE PAIN

Acute pain, sudden in onset and lasting less than 1 month, may be viewed as an expected physiologic response to a noxious stimulus (such as injury, trauma, or surgery). However, inadequately or ineffectively treated pain has serious consequences, including delayed recovery, increased health care utilization, and prolonged postsurgical recovery. Unresolved acute pain can progress to subacute pain (lasting 1 to 3 months) and then to chronic pain, which typically lasts more than 3 months.[10,11]

Acute pain management today incorporates the 2022 CDC guidelines, outlining treatment decisions based on function rather than pain scores alone and individualized multimodal nonopioid or opioid-sparing treatment plans.[2] Nonpharmacologic strategies, including early mobilization and guided activity, remain essential complements to pharmacologic care.[7,12] Selective $Na_V1.8$ inhibitors have the potential to be integral to these plans.

BOX 2. Local anesthetics vs $Na_V1.8$ inhibitors: a mechanistic distinction.

Lidocaine and other traditional local anesthetics are nonselective sodium channel blockers affecting multiple channel subtypes throughout the body, limiting their systemic use due to dose-dependent cardiovascular and CNS toxicity.[13] In contrast, suzetrigine is a highly selective $Na_V1.8$ inhibitor targeting sodium channels predominantly expressed on peripheral nociceptive neurons, C-fibers. This peripheral selectivity enables oral, mechanism-based analgesia for moderate-to-severe acute pain without engaging opioid receptors or resulting in the systemic toxicity associated with nonselective sodium channel blockade.[8] Genetic studies of SCN10A, the gene encoding $Na_V1.8$, further support this target: gain-of-function variants are associated with increased pain sensitivity, whereas loss-of-function variants are linked to reduced pain perception.[14]

Initial evaluation: brief framework

Step 1: Structured evaluation of medical and psychosocial factors influencing the patient's pain. The primary goal is to identify and address the underlying cause of pain.[7] When the cause cannot be eliminated immediately or if pain persists despite treatment, classify the pain mechanism as nociceptive, inflammatory, neuropathic, or mixed to guide analgesic selection.[7,8]

Step 2: Using a shared decision-making process, create a plan focused on functional improvement, minimizing unnecessary opioid use, and outline follow-up steps for clinical deterioration or unexpected responses (see **FIGURE 1**). [7,15]

CASE STUDY 1

Maria R., a 44-year-old teacher, presents 4 days after arthroscopic rotator cuff repair with persistent postoperative pain. She was discharged on oxycodone 5 mg every 6 hours as needed and acetaminophen 650 mg every 6 hours, also as needed. Her medical history includes hypertension, obesity, and remote postpartum depression.

She reports pain severity of 8/10 at its worst and about 5/10 at rest, taking approximately 3 oxycodone tablets daily. She describes opioid-related adverse effects, including sedation and nausea, and expresses significant anxiety about opioid use. She notes her brother struggled with opioid addiction after being prescribed oxycodone, and she worries about heading down "that same path."

She messaged her surgeon and was told to maximize the oxycodone use for the next 3 days, and keep her scheduled postoperative appointment the following week. Uncomfortable with this plan, she turns to her PCC for help with nonopoid pain management.

On examination, vital signs are stable, aside from mildly elevated blood pressure. The surgical site appears appropriate for postoperative day 4.

Gaps in current care

Her analgesics are being used reactively rather than on a scheduled basis—a common but suboptimal pattern that allows pain to escalate before treatment. The American Society of Anesthesiologists recommends that, unless contraindicated, patients receive a scheduled regimen of an NSAID (nonselective or COX-2 selective), with or without acetaminophen. This proactive approach is well supported and helps maintain more consistent analgesia, reduce peak pain intensity, and limit the need for rescue medications.[16]

Maria has no renal, gastrointestinal, or hepatic issues, so she can use first-line therapies.

The plan

- Acetaminophen 1000 mg every 6 hours, an NSAID if blood pressure remains controlled, ice and guided mobilization, and oxycodone for breakthrough pain only.

Why her concerns matter clinically

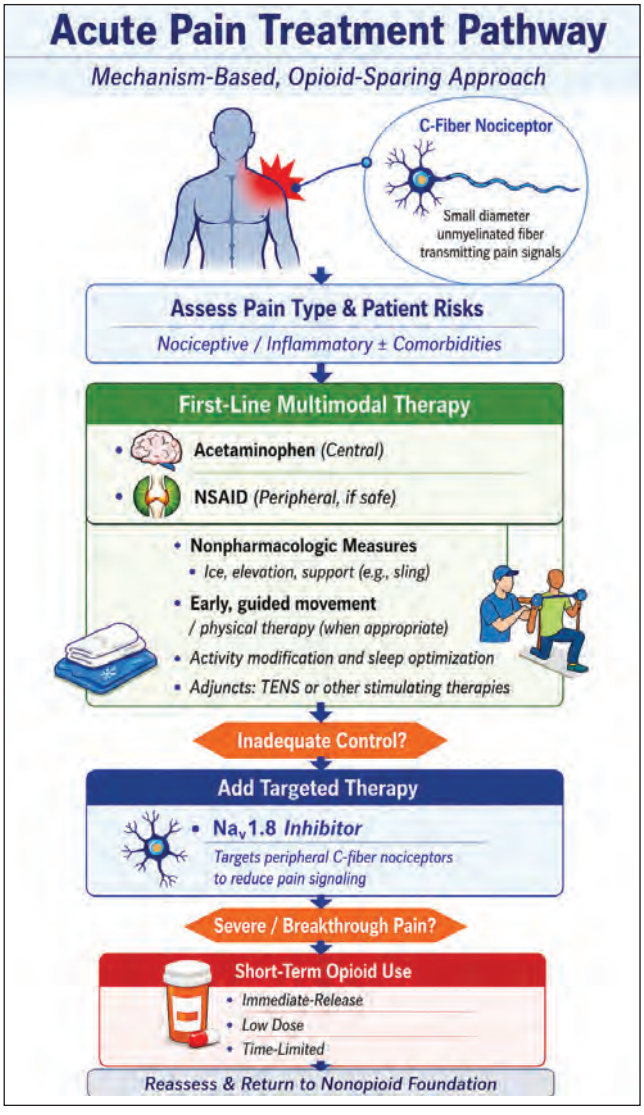
The 2022 CDC guideline highlights that patient preferences, values, and goals should guide prescribing, and effective communication about pain expectations and treatment length boosts adherence to nonopioid strategies. Treatment should focus on functional improvement—sleep, dressing, returning to work—rather than complete pain elimination.[7]

A NEW OPTION

For a patient wanting to reduce opioid exposure and suffering adverse effects, the usual approach was to optimize acetaminophen and NSAIDs. Suzetrigine offers a different, peripherally targeted mechanism, selectively inhibiting $Na_V1.8$ sodium channels on C-fiber nociceptive neurons, potentially replacing opioids rather than supplementing them (see **FIGURE 2**).[8]

The FDA approval was based on two phase 3, randomized, double-blind trials evaluating suzetrigine for acute postoperative pain after abdominoplasty and bunionectomy, with 2191 adults enrolled across the studies. Suzetrigine was administered as a 100 mg loading dose on an empty stomach to avoid delayed onset, followed by 50 mg every 12 hours.

FIGURE 1. Mechanism-based approach to acute pain management.



Abbreviation: TENS, transcutaneous electrical nerve stimulation.

In both surgical models, suzetrigine produced statistically significant pain reduction compared with placebo (P <.001 for abdominoplasty; P =.0002 for bunionectomy), supporting its role as an effective nonopioid analgesic option. Available comparative data suggest its analgesic effect is broadly in the range of NSAIDs, while slightly lower than higher-dose opioid regimens. Direct claims of equivalence or superiority to hydrocodone/acetaminophen should be avoided because the pivotal trials were not designed or powered to establish opioid noninferiority or superiority, and comparator findings were not fully consistent across models.[17]

Discontinuation rates due to lack of efficacy were substantially higher in the placebo group (22% after abdominoplasty and 16% after bunionectomy) than in the suzetrigine group (9% and 12%, respectively), and overall completion rates were lower in placebo patients (75% and 82%) than in suzetrigine patients (89% and 87%).[8,17] These differences, while not formally tested for statistical significance, are directionally consistent across all models and suggest a clinically relevant advantage in treatment persistence with suzetrigine, particularly in the abdominoplasty model, where the difference was most pronounced.[8,17]

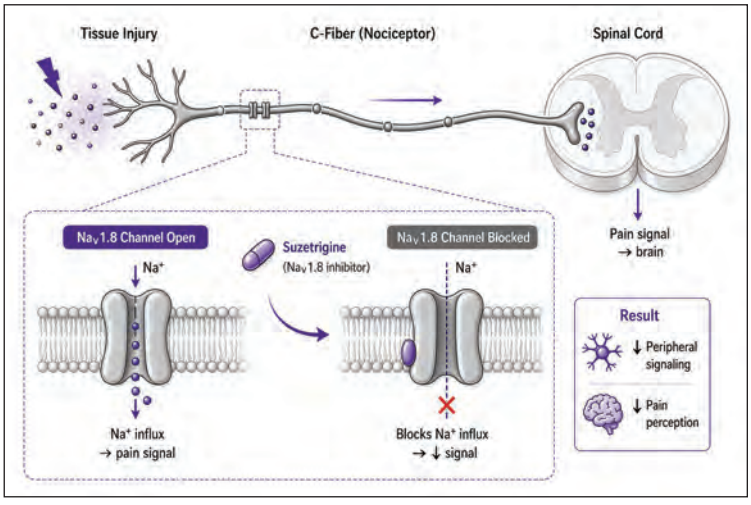
The average age of participants in the trials was mid-40s. The trials were short-term and looked only at acute pain relief over 48 hours. Approval is based on safety data up to 14 days.[8,17]

A 2026 meta-analysis of 4 randomized datasets (N=1584) found statistically significant pain reduction with suzetrigine vs placebo at 24 hours (mean difference –0.93 on a scale; 95% confidence interval [CI]: –1.38, –0.48) and 48 hours (mean difference –1.02; 95% CI: –1.32, –0.72). A separate 2026 meta-analysis of 5 randomized controlled trials (RCTs) (N=2855) similarly found improved 48-hour summed pain intensity difference vs placebo, with fewer adverse events than placebo or hydrocodone/acetaminophen and no superiority in pain relief vs hydrocodone/acetaminophen. Overall, suzetrigine shows consistent short-term analgesic benefit vs placebo, but opioid-sparing conclusions remain limited because opioid consumption was not consistently reported.[18,19]

A separate, phase 3, single-arm open-label study (N=256) evaluated suzetrigine across surgical and nonsurgical moderate-to-severe acute pain conditions. Using a 5-point patient global assessment scale (poor, fair, good, very good, or excellent), 83.2% of all participants rated suzetrigine's effectiveness as good, very good, or excellent at the end of treatment; this included 82.0% of surgical participants and 91.2% of nonsurgical participants.[20]

In Case Study 1, Maria strongly prefers to stop opioids; therefore, suzetrigine is a reasonable option to consider. It is important to discuss the 14-day maximum use (which should fit Maria's postoperative course). Shared decision-making frames treatment around functional recovery and patient goals, with timely follow-up to reassess benefit, tolerability, and progress. A clear plan to taper and discontinue all acute analgesics as recovery advances reinforces that the goal is short-term support rather than ongoing medication use. Communication with her surgeon about her concerns regarding opioids and the revised analgesic plan support continuity of care.[3]

FIGURE 2. Mechanism of action of selective $Na_V1.8$ inhibition in acute pain.



Tissue injury activates peripheral nociceptors through inflammatory mediators. $Na_V1.8$ contributes to action potential upstroke and sustained firing. Suzetrigine blocks $Na_V1.8$ channels, reducing pain signal transmission. The result is attenuated pain transmission from the peripheral nerve to the spinal cord.[22,23]

PRESCRIBING CONSIDERATIONS AND SIDE EFFECTS

Most reported side effects of suzetrigine were mild and included pruritus, muscle spasms, and rash. Although nausea and vomiting were reported, these occurred at a significantly lower rate than with the opioid comparator and were even lower than placebo in both surgical models.[17-20]

Suzetrigine is primarily metabolized by cytochrome P450, family 3, subfamily A (CYP3A) (mainly CYP3A4) and also induces CYP3A. Clinically, this means it should not be used with strong CYP3A inhibitors, while moderate CYP3A inhibitors require dose reduction. On the other hand, strong or moderate CYP3A inducers may markedly reduce suzetrigine concentrations, potentially resulting in a loss of efficacy. Remind patients to avoid grapefruit because of potential CYP-mediated interactions, and in relevant cases, discuss that suzetrigine could limit the effectiveness of certain oral contraceptives.[7,8]

No dose adjustment is required for mild hepatic impairment. For moderate hepatic impairment, the recommended regimen is 100 mg initially on an empty stomach, followed by 50 mg every 12 hours for doses 2 through 4, then 50 mg every 24 hours thereafter. Suzetrigine should be avoided in severe hepatic impairment, as it has not been studied in this population. Routine hepatic laboratory monitoring is not recommended in the Prescribing Information, although clinical reassessment is appropriate if symptoms or laboratory abnormalities suggest liver injury.[6,8,21]

Clinical Takeaway: Scheduled multimodal nonopioid therapy remains the core of acute pain management. If acetaminophen and NSAIDs are inadequate, clinicians may consider suzetrigine to reduce opioid exposure.

CASE STUDY 2

James L., a 59-year-old construction worker, presents 2 days after an acute low back injury.

His medical history includes stage 3 chronic kidney disease (estimated glomerular filtration rate [eGFR] 48 mL/min/1.73 m^2), type 2 diabetes, hypertension, chronic low back pain previously treated with tramadol, and alcohol use disorder in remission. He prefers to avoid medications with dependence risk.

Chronic medications: metformin, sodium-glucose cotransporter 2 inhibitor, ACE inhibitor, and a statin.

On examination, he demonstrates guarded movement, focal paraspinal tenderness, and muscle spasm without neurologic deficit. James exemplifies a typical primary care case: a patient with comorbidities that eliminate first-line options. Chronic kidney disease makes NSAIDs risky.[3,4] James wants to avoid medications with dependence potential, making opioid therapy less appealing.[3] Acetaminophen is renal safe but less effective for low back pain.[24,25]

Where suzetrigine fits

Suzetrigine avoids NSAID renal and gastrointestinal toxicity and opioid CNS effects, respiratory depression, and addiction due to its peripheral action.[5,6] The FDA label requires no renal dose adjustment for patients with eGFR ≥15 mL/min/1.73 m^2. However, in the pivotal trials, eGFR decreases of ≥25% (but <50%) occurred in 2.5% of suzetrigine patients vs 0.9% on placebo; these appeared to resolve after discontinuation in the open-label, phase 3 study. Safety in patients with eGFR <15 mL/min or on dialysis has not been studied, and baseline monitoring of renal function is prudent in patients with CKD.[17,20,21]

The pivotal RCTs were in postoperative models, not acute low back pain.[6] The phase 3, open-label study (see Maria's case) included surgical and nonsurgical acute pain.[20] Highlighting potential benefits and suzetrigine data on related conditions supports shared decision-making and a comprehensive approach.

The plan

- Superficial heat and early guided mobilization
- Suzetrigine 100 mg loading dose on an empty stomach, then 50 mg every 12 hours (short term)
  - Consider a consult with a clinical pharmacist (review medication list for CYP3A interactions and consider changing the statin: simvastatin and lovastatin are most susceptible)[26]
- Short-course cyclobenzaprine 5 to 10 mg at bedtime if spasm is prominent
- Acetaminophen 650 to 1000 mg every 6 hours as adjunctive, recognizing limited efficacy for low back pain
- Opioids avoided given substance use disorder history and patient preference; if severe breakthrough pain is present, a brief course could be used with close follow-up per CDC guideline

Treatment goals: ability to sit comfortably, return to modified work duties, and progressive increase in activity tolerance.

Suzetrigine's 14-day maximum studied duration provides a built-in endpoint. Reassess at 3 to 5 days to evaluate functional improvement (not simply whether pain persists) and include diagnostic reassessment rather than dose escalation if goals are unmet.[6-8]

Clinical Takeaway: When comorbidities eliminate first-line options, mechanism-based thinking reveals new pathways.

CASE STUDY 3

Danielle M., a 52-year-old business owner in a rural area, presents 6 days after bunion surgery with persistent pain. At her postoperative appointment she was told healing was on track and advised to discontinue oxycodone. She reports pain persisting from 3/10 at rest to 6/10 with movement, despite scheduled acetaminophen and ibuprofen and nonpharmacologic care. The pain is draining and affecting sleep. She wonders, "Isn't there something else to try?"

Practical opioid stewardship in acute pain

Opioid stewardship means using opioids deliberately, briefly, and with defined goals, not eliminating them.

Key principles: reserve opioids for severe pain after nonopioid optimization; prescribe immediate-release formulations in limited quantities; establish functional goals and an exit strategy at initiation; review Prescription Drug Monitoring Program data; and avoid concurrent benzodiazepines.[7]

Danielle's clinical scenario, moderate-to-severe postoperative pain after bunionectomy with opioid intolerance, aligns closely with the pivotal trial population.[17]

The plan

- Continue scheduled acetaminophen and ibuprofen
- Add suzetrigine 100 mg loading dose on an empty stomach, then 50 mg every 12 hours (short term)
- Restrict oxycodone to severe breakthrough pain only, with an explicit exit strategy
- Continue nonpharmacologic measures: icing, elevation, and gradual mobilization
- Follow up in 1 to 2 weeks to assess functional improvement and de-escalate therapies

Treatment goals: ability to bear weight comfortably, return to normal footwear, and progressively increase walking tolerance.

Clinical Takeaway: Suzetrigine offers a nonopioid alternative for patients with moderate-to-severe acute pain who are intolerant of opioids, with pain reduction comparable to hydrocodone/acetaminophen and lower rates of nausea and dizziness.

SUMMARY

Acute pain care is evolving, yet the primary care goal remains consistant: relieve pain, restore function, and reduce downstream harm. Suzetirgine adds a targeted nonopioid option within multimodal care, especially when opioid risks, intolerance, or patient preference make opioid-sparing strategies important.

Optimal treatment still depends on structured assessment, mechanism-informed medication choice, nonpharmacologic recovery strategies, functional goals, follow-up, and careful opioid stewardship when opioids are used. ●

REFERENCES

1. St Sauver JL, Warner DO, Yawn BP, et al. Why patients visit their doctors: assessing the most prevalent conditions in a defined American population. *Mayo Clin Proc*. 2013;88(1):56-67. https://doi.org/10.1016/j.mayocp.2012.08.020
2. Finley CR, Chan DS, Garrison S, et al. What are the most common conditions in primary care? Systematic review. *Can Fam Physician*. 2018;64(11):832-840. https://www.cfp.ca/content/64/11/832.long
3. Alorfi NM. Pharmacological methods of pain management: narrative review of medication used. *Int J Gen Med*. 2023;16:3247-3256. https://doi.org/10.2147/ijgm.s419239
4. Paul AK, Smith CM, Rahmatullah M, et al. Opioid analgesia and opioid-induced adverse effects: a review. *Pharmaceuticals (Basel)*. 2021;14(11):1091. https://doi.org/10.3390/ph14111091
5. Hochberg MC. NSAIDs: mechanisms and pathways of action. *Hosp Pract*. 1989;24(3):185-198. https://doi.org/10.1080/21548331.1989.11703684
6. Keam SJ. Suzetrigine: first approval. *Drugs*. 2025;85(6):845-851. https://doi.org/10.1007/s40265-025-02178-w
7. Dowell D, Ragan KR, Jones CM, Baldwin GT, Chou R. CDC clinical practice guideline for prescribing opioids for pain—United States, 2022. *MMWR Recomm Rep*. 2022;71(RR-3):1-95. https://doi.org/10.15585/mmwr.rr7103a1
8. Mach M, Giba A, Miedziaszczyk M, et al. Suzetrigine as a novel nonopioid analgesic drug in pain management: a review of clinical evidence and therapeutic perspectives. *Cureus*. 2025;17(8):e90755. https://doi.org/10.7759/cureus.90755
9. Brune K. Next generation of everyday analgesics. *Am J Ther*. 2002;9(3):215-223. doi:10.1097/00045391-200205000-00007
10. Glare P, Aubrey KR, Myles PS. Transition from acute to chronic pain after surgery. *The Lancet*. 2019;393(10180):1537-1546. https://doi.org/10.1016/s0140-6736(19)30352-6
11. Kehlet H, Jensen TS, Woolf CJ. Persistent postsurgical pain: risk factors and prevention. *The Lancet*. 2006;367(9522):1618-1625. https://doi.org/10.1016/s0140-6736(06)68700-x
12. Qaseem A, Wilt TJ, McLean RM, Forciea MA; Clinical Guidelines Committee of the American College of Physicians. Noninvasive treatments for acute, subacute, and chronic low backpain: a clinical practice guideline. *Ann Intern Med*. 2017;166(7):514-530. https://doi.org/10.7326/m16-2367
13. Körner J, Albani S, Sudha Bhagavath Eswaran V, et al. Sodium channels and local anesthetics — old friends with new perspectives. *Front Pharmacol*. 2022;13:837088. doi:10.3389/fphar.2022.837088.
14. Waxman SG, Merkies ISJ, Gerrits MM, et al. Sodium channel genes in pain-related disorders: phenotype-genotype associations and recommendations for clinical use. *The Lancet Neurol*. 2014;13(11):1152-1160. doi:10.1016/S1474-4422(14)70150-4
15. Bello CM, Mackert S, Harnik MA, Filipovic MG, Urman RD, Luedi MM. Shared decision-making in acute pain services. *Curr Pain Headache Rep*. 2023;27(7):193-202. doi:10.1007/s11916-023-01111-8
16. American Society of Anesthesiologists Task Force on Acute Pain Management. Practice guidelines for acute pain management in the perioperative setting: an updated report by the American Society of Anesthesiologists Task Force on Acute Pain Management. *Anesthesiology*. 2012;116(2):248-273. https://doi.org/10.1097/aln.0b013e31823c1030
17. Bertoch T, D'Aunno D, McCoun J, et al. Suzetrigine, a nonopioid NaV1.8 inhibitor for treatment of moderate-to-severe acute pain: two phase 3 randomized clinical trials. *Anesthesiology*. 2025;142(6):1085-1099. https://doi.org/10.1097/aln.0000000000005460
18. Alvarez-Aguilar P, Picado-Loaiza S. Suzetrigine (a NaV1.8 inhibitor) versus placebo for acute postoperative pain: a systematic review and meta-analysis of randomized controlled trials. *Medicine (Baltimore)*. 2026;105(10):e47877. https://doi.org/10.1097/md.0000000000047877
19. Irfan Q, Zaidi SMM, Zohair M, et al. Safety and efficacy of suzetrigine (VX-548) for acute moderate to severe pain in adults: a systematic review and meta-analysis. *J Clin Anesth*. 2026;111:112156. https://doi.org/10.1016/j.jclinane.2026.112156
20. McCoun J, Winkle P, Solanki D, et al. Suzetrigine, a nonopioid NaV1.8 inhibitor with broad applicability for moderate-to-severe acute pain: a phase 3 single-arm study. *J Pain Res*. 2025;18:1569-1576. https://doi.org/10.2147/jpr.s509144
21. Journavx (suzetrigine). Prescribing Information. Vertex Pharmaceuticals Inc.; January 2026. Accessed September 7, 2026. https://pi.vrtx.com/files/uspi_suzetrigine.pdf
22. Chen R, Liu Y, Qian L, et al. Sodium channels as a new target for pain treatment. *Front Pharmacol*. 2025;16:1573254. https://doi.org/10.3389/fphar.2025.1573254
23. Dib-Hajj SD, Cummins TR, Black JA, Waxman SG. Sodium channels in normal and pathological pain. *Annu Rev Neurosci*. 2010;33:325-347. doi:10.1146/annurev-neuro-060909-153234.
24. Saragiotto BT, Machado GC, Ferreira ML, Pinheiro MB, Sheheed CA, Maher CG. Paracetamol for low back pain. *Cochrane Database Syst Rev*. 2016;(6):CD012230.
25. US Department of Veterans Affairs, Department of Defense. VA/DoD Clinical Practice Guideline for the Diagnosis and Treatment of Low Back Pain. Version 3.0. US Dept of Veterans Affairs; 2022. Accessed June 7, 2026. https://www.healthquality.va.gov/HEALTHQUALITY/guidelines/Pain/lbp/VADODLBPCPGFinal508.pdf
26. Wiggins BS, Saseen JJ, Page RL II, et al. Recommendations for management of clinically significant drug-drug interactions with statins and select agents used in patients with cardiovascular disease: a scientific statement from the American Heart Association. *Circulation*. 2016;134(21):e468-e495. doi:10.1161/CIR.0000000000000456