"Making Waves"
25th Annual Pain Medicine Meeting
November 5-7, 2026 | Tampa, Florida
ASRA PAIN MEDICINE

A Literature Review of Suzetrigine for Neuropathic Pain

Justin Baik, MD[1], Stephanie Batarseh, MD[1], Hein Thant, MD[2], Samuel Thampi, MD[1]

1. Department of Physical Medicine and Rehabilitation, One Brooklyn Health System, Brooklyn, NY
2. Department of Pain Medicine, Rutgers NJMS, Somerset, NJ

Introduction

Suzetrigine (VX-548) is a first-in-class, orally bioavailable selective inhibitor of the NaV1.8 voltage-gated sodium channel, which is expressed almost exclusively in peripheral dorsal root ganglion (DRG) nociceptors and provides the majority of the depolarizing current required for repetitive action-potential firing in these neurons. FDA approval in January 2025 was based solely on pivotal Phase 3 trials in acute nociceptive, postoperative pain following abdominoplasty and bunionectomy; this remains suzetrigine's only approved indication.

Given NaV1.8's role in dorsal root ganglion nociceptor excitability, suzetrigine has since been investigated off-label in several peripheral neuropathic pain conditions, with divergent early results. No systematic synthesis of this expanding neuropathic pain evidence base exists. We conducted a review to map available clinical evidence, identify research gaps, and provide practical guidance for PM&R and pain physicians.

Methods

Search Engines: MEDLINE, EMBASE, Cochrane Library, and PubMed.

Keywords: ("suzetrigine" OR "VX-548") AND ("neuropathic pain") paired with 11 conditions (DPN, LSR, PHN, TN, CRPS, PLP, SFN, CIPN, CPSP, SCI, MS).

Exclusion: Acute nociceptive trials excluded.

Disclosures & Ethics

- COI: Authors declare no conflicts of interest.
- IRB: Exempt per OBH policy (devoid of patient data).
- Off-Label: Off-label neuropathic review analyzed.

Results

Condition	Study / Design	Intervention	Key Findings & Outcomes
DPN	Freeman et al. (2025) Phase 2 RCT (n=192)	Suzetrigine (3 doses) vs. Pregabalin ref.	Significant pain score reduction at all doses; efficacy comparable to pregabalin.
LSR	Vertex / Zeng (2025/26) Phase 2 RCT (n=218)	Suzetrigine vs. Placebo	Did NOT achieve statistical superiority over placebo (primary endpoint missed).
HSN	Nimma et al. (2025) Case Report (n=1)	Suzetrigine Postop regimen	Successful postop pain control in adolescent with hereditary sensory neuropathy.
Other (6 conditions)	Systematic Gap Analysis	PHN, TN, CRPS, CPSP, SCI, MS	**Zero clinical data published to date.** Classified as unproven / experimental.

Discussion

These findings suggest suzetrigine's efficacy tracks peripheral versus central sensitization: DPN, a peripheral process, responded favorably, while LSR, which often involves central sensitization from nerve root compression, did not separate from placebo. Since NaV1.8 is expressed primarily in peripheral dorsal root ganglion neurons with minimal CNS distribution, biological plausibility is stronger for peripherally-driven conditions (postherpetic neuralgia, trigeminal neuralgia, CRPS) than centrally-mediated ones (post-stroke, spinal cord injury, multiple sclerosis pain); none of these six have been studied directly.

Clinically, a tiered approach is warranted. Suzetrigine's only FDA-approved indication is acute postoperative pain (abdominoplasty, bunionectomy); neuropathic use is off-label. DPN has evidence-backed support from a positive Phase 2 trial. LSR carries a negative pivotal trial, tempering expectations. The remaining conditions, postherpetic neuralgia, trigeminal neuralgia, CRPS, central post-stroke pain, spinal cord injury pain, and MS pain, have zero suzetrigine-specific data and should be considered experimental, warranting explicit informed consent or trial referral. Further study is needed to define suzetrigine's role across these conditions.

References

1.. Alsaloum M, Dib-Hajj SD, Page DA, Ruben PC, Krainer AR, Waxman SG. Voltage-gated sodium channels in excitable cells as drug targets. Nat Rev Drug Discov. 2025 May 1;24(5):358. doi:10.1038/S41573-024-01108-X PubMed PMID: 39901031.
2. Bertoch T, D'Aunno D, McCoun J, Solanki D, Taber L, Urban J, et al. Suzetrigine, a Nonopioid Na V 1.8 Inhibitor for Treatment of Moderate-to-severe Acute Pain: Two Phase 3 Randomized Clinical Trials. Anesthesiology. 2025 Jun 1;142(6):1085–99. doi:10.1097/ALN.0000000000005460 PubMed PMID: 40117446.
3. Jones J, Correll DJ, Lechner SM, Jazic I, Miao X, Shaw D, et al. Selective Inhibition of Na V 1.8 with VX-548 for Acute Pain . New England Journal of Medicine. 2023 Aug 3;389(5):393–405. doi:10.1056/NEJMOA2209870;REQUESTEDJOURNAL:JOURNAL:NEJM;PAGE:STRING:ARTICLE/CHAPTER PubMed PMID: 37530822.
4. Freeman R, Rauck R, Argoff C, Tian S, Miao X, Olivet HB, et al. Suzetrigine, a Selective Pain Signal Inhibitor of NaV1.8 Shows Proof-of-concept for Treatment of Painful Diabetic Peripheral Neuropathy (S11.002). Neurology. 2025 Apr 8;104(7_Supplement_1):3054. doi:10.1212/WNL.0000000000210760
5. Zeng X, Powell R, Woolf CJ. Mechanism-based nonopioid analgesic targets. J Clin Invest. 2025 Jun 2;135(11):e191346. doi:10.1172/JCI191346 PubMed PMID: 40454476.
6. Vertex Pharmaceuticals | Vertex Announces Results From Phase 2 Study of Suzetrigine for the Treatment of Painful Lumbosacral Radiculopathy [Internet]. [cited 2026 Jul 23]. Available from: https://investors.vrtx.com/news-releases/news-release-details/vertex-announces-results-phase-2-study-suzetrigine-treatment
7. Nimma SR, Kivanc TY, Colontonio MM. Use of Suzetrigine, a Selective Sodium Channel Blocker, in Postoperative Pain Management for an Adolescent Patient With Hereditary Neuropathy: A Case Report. A A Pract. 2025;19(12):e02114. doi:10.1213/XAA.0000000000002114 PubMed PMID: 41335035.
8. Hameed S. Nav1.7 and Nav1.8: Role in the pathophysiology of pain. Mol Pain. 2019 Jun 1;15:1744806919858801. doi:10.1177/1744806919858801 PubMed PMID: 31172839.