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Suzetrigine: A First-in-Class Non-Opioid Analgesic — Promise With Vigilance

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Suzetrigine (brand name Journavx) is a recently approved, first-in-class, oral, non-opioid analgesic indicated for the treatment of moderate to severe acute pain in adults. Approved by the U.S. Food and Drug Administration (FDA) in 2025, it represents the first novel mechanistic class of oral analgesic in more than two decades.[1]

For clinicians practicing in post-acute and long-term care settings, its arrival is significant. It offers a targeted, peripherally acting alternative to opioids at a time when opioid stewardship remains central to safe pain management in older adults.

Mechanism of Action and Pharmacology

Suzetrigine is a highly selective inhibitor of the voltage-gated sodium channel NaV1.8, expressed predominantly on peripheral nociceptive neurons.[2] By stabilizing this channel in a nonconducting state, suzetrigine interrupts potential propagation along pain fibers before signals reach the central nervous system.

This mechanism differs fundamentally from:

- Opioids, which activate central μ-receptors
- NSAIDs, which inhibit prostaglandin synthesis

- Centrally acting agents such as tramadol, which combine weak opioid agonism with monoaminergic effects[3]

Because NaV1.8 is largely confined to peripheral sensory neurons, suzetrigine demonstrates minimal CNS penetration and has not been associated with respiratory depression, addiction, or euphoric effects in clinical trials.[1,4]

Pharmacologic characteristics include:

- Oral administration; while it is recommended to be taken whole on an empty stomach, data exist to support bioavailability upon crushing for adults with swallowing disorders[4]
- Twice-daily dosing
- No opioid receptor activity
- No demonstrated respiratory depression
- No known addictive signal in clinical trials[1,4]

Indications

Suzetrigine is approved for moderate to severe acute pain in adults.[1] Its safety and efficacy in chronic pain or extended use (beyond 14 days) remain under investigation. At present, it should be viewed as an acute pain therapy rather than a chronic daily analgesic.

Studies in Product Information

- In two studies of acute post-operative pain, one following bunionectomy and the other following abdominoplasty, suzetrigine demonstrated statistically significant and clinically meaningful reductions in pain intensity compared with placebo at 48 hours.[4]
- However, the studies did not demonstrate superiority over a standard opioid/acetaminophen combination (hydrocodone/acetaminophen) on key secondary endpoints in these trials. Hydrocodone/ acetaminophen became increasingly effective after the first 48 hours.[4]
- All trials permitted “rescue” ibuprofen for inadequate pain control, reflecting real-world adjunctive use.
- The average age of study participants was in their 40s. As with most clinical studies, patients typical of the age and having the comorbidities seen in post-acute and long-term care were excluded.

In both studies, suzetrigine was generally well tolerated, and adverse events were mostly mild to moderate.[3]

- A 12-week study of patients with lumbosacral radiculopathy showed a clinically meaningful within-group reduction in pain on the numeric pain rating scale (NPRS) with suzetrigine, but the magnitude of reduction was similar to the placebo group.[5]

Adverse Reactions

Across phase 2 and phase 3 trials, suzetrigine demonstrated a generally favorable safety profile.[1,4] Reported adverse effects include:

- Pruritus
- Rash
- Muscle spasms
- Elevated creatine kinase (CK)

Importantly, trials have not demonstrated:

- Respiratory depression
- Sedation or delirium signal
- Evidence of misuse liability[1]

CK elevations warrant consideration in frail older adults, particularly those receiving statins or at elevated fall risk.

As with any newly approved medication, continued post-marketing surveillance will be critical in defining long-term safety.

Contraindications and Drug Interactions

Suzetrigine is metabolized primarily via CYP3A pathways.[1]

Contraindicated:

- Concomitant use with strong CYP3A inhibitors (e.g., clarithromycin, ketoconazole, ritonavir)

Avoid or use caution:

- Strong CYP3A inducers (e.g., rifampin, carbamazepine, phenytoin) due to reduced efficacy

- Moderate CYP3A inhibitors (e.g., diltiazem, verapamil, fluconazole)
- Avoid food or drink containing grapefruit during treatment

Additional cautions include:

- Severe hepatic impairment[1]
- Limited data in patients with eGFR < 15 mL/min, including those undergoing dialysis
- Polypharmacy common in skilled nursing facilities

Cost and Access

The wholesale acquisition cost is approximately $15.50 per 50-mg tablet, translating to roughly $30 per day at typical dosing.[1] Retail pricing for short courses may exceed several hundred dollars without insurance.

Coverage varies:

- Commercial plans often require prior authorization
- Medicare Part D coverage is inconsistent and frequently tiered at higher cost-sharing levels
- Medicaid coverage varies by state

In long-term care settings, formulary placement and managed care contracting will strongly influence adoption.

Clinical Implications for Post-Acute and Long-Term Care

Suzetrigine may offer particular value in:

- Postoperative patients at high risk for opioid-related delirium
- Residents with chronic kidney disease limiting NSAID use
- Multimodal opioid-sparing protocols
- Residents with opioid use disorder for whom the use of opioids is not ideal

Caution remains appropriate in:

- Chronic daily pain syndromes
- Hospice settings requiring rapid titration

- Cost-sensitive populations without reliable coverage

Suzetrigine represents a meaningful pharmacologic innovation in acute pain management. For geriatric and palliative clinicians, thoughtful patient selection, attention to drug interactions, and careful monitoring will determine its appropriate role in practice.

Cautionary Note

In prior analgesic cycles—including agents such as Propoxyphene, Pentazocine (Talwin) and Rofecoxib—early warning signs were typically evident within years of market entry, yet corrective action at the system level frequently lagged by decades.

References

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