INSTRUCTIONS TO FIELD REVIEWERS

Suzetrigine (JOURNAVX) in Moderate to Severe Acute Pain
National Drug Mini-monograph
May 2025

VA Pharmacy Benefits Management Services and National Formulary Committee

The purpose of VA National Formulary Committee drug monographs is to provide a focused drug review for making formulary decisions. The Product Information or other resources should be consulted for detailed and most current drug information.

FDA APPROVAL INFORMATION	
Description / MOA	Non-opioid analgesic/ Sodium Channel Blocker, NaV1.8 Selective
Indication Under Review[1]	Treatment of moderate to severe acute pain in adults
Dosage Regimen	Loading dose: 100 mg on empty stomach; Subsequent doses: 12 hours after loading dose start maintenance dose of 50 mg every 12 hours
Dosage Forms Under Review	Tablet for oral use

EFFICACY CONSIDERATIONS		
Trial	**Study VX22-548-104 A Phase 3, Randomized, Double-blind, Placebo-controlled Study Evaluating the Efficacy and Safety of Suzetrigine for Acute Pain After a Bunionectomy**	**Study VX22-548-105: A Phase 3, Randomized, Double-blind, Placebo-controlled Study Evaluating the Efficacy and Safety of Suzetrigine for Acute Pain After an Abdominoplasty**
Design	R, DB, Placebo and Active control trial	R, DB, Placebo and Active control trial
Population	1075 adults (primarily women - 85%) with pain score >4/10 after bunionectomy procedure and 9 hours after anesthetic block removal	1118 adults (99% women) undergoing abdominoplasty reporting pain score >4/10 four hours after surgery complete.
Intervention	Suzetrigine high dose (100mg x1 then 50mg q12h), medium dose (60mgX1 then 30mg q12h) or low dose (20mgx1 then 10mg q12h) for 48 hours	Suzetrigine high dose (100mg x1 then 50mg q12h), medium dose (60mgX1 then 30mg q12h) for 48 hours
Comparator	Hydrocodone/APAP 5/325 q6h or placebo. (NOTE: Use of other drugs or ice-packs not allowed except ibuprofen 400mg as rescue medication)	Hydrocodone/APAP 5/325 q6h or placebo. (NOTE: Use of other drugs or ice-packs not allowed except ibuprofen 400mg as rescue medication)
Results	Primary outcome of SPID48 with VX548 50mg bid vs. placebo demonstrated greater magnitude of change at a statistically significant level [SPID48 LS mean (SE) placebo 70.6 (6.3); suzetrigine 99.9 (4.5) SPID48 LS mean difference from placebo 29.3 95% CI (14.0, 44.6) P value vs. placebo 0.0002]. Key secondary endpoint of SPID48 versus HC/APAP favored HC/APAP over suzetrigine	Primary outcome of SPID48 with VX548 50mg bid vs. placebo demonstrated greater magnitude of change at a statistically significant level [SPID48 LS mean (SE) placebo 70.1 (6.1); suzetrigine 118.4 (4.3) SPID48 LS mean difference from placebo 48.4 95% CI (33.6, 63.1) P value vs. placebo <0.0001]. Key secondary endpoint of SPID48 versus HC/APAP found no statistical difference between suzetrigine and active control.

SAFETY CONSIDERATIONS	
Boxed Warnings	None
Contraindications	Concomitant use with strong CYP3A4 inhibitors.
Other Warnings	Patients using contraceptives containing progestins other than levonorgestrel and norethindrone require additional nonhormonal contraception (e.g., condoms) or alternative contraceptives during suzetrigine therapy and for 28 days after the last dose.
Top 5 AEs	Skin rash (1%), Increased creatine phosphokinase in blood specimen (1% to 3%), muscle spasm (1%), Decreased estimated GFR (eGFR) (3%)
Drug Interactions	CYP3A4 inhibitors may increase the serum concentration of suzetrigine. CYP3A4 inducers may decrease the serum concentration of suzetrigine. Suzetrigine may decrease serum concentration of hormonal contraceptives.

VHA PLACE IN THERAPY		
	Potential Use in VHA	Suzetrigine is the first novel mechanism of action analgesic approved in decades. In acute, post-operative pain it has a modest reduction in pain, with a small effect size that is numerically better than placebo. However, the clinical significance of this difference is uncertain (e.g. similar request for rescue med use versus placebo). Suzetrigine did not perform better than low-dose opioid therapy (e.g. 20 MEDD), was not studied in context of usual post-operative pain protocols and was studied primarily in middle-aged females. As such, generalizability to how a VHA Veteran population would respond to treatment is unclear. Suzetrigine is currently only indicated as a treatment for acute pain. While mechanism of action is novel and it did perform better versus placebo, there is not evidence that it performs better than treatment options commonly used postoperatively and already on formulary (e.g. NSAIDs, intravenous APAP, opioids, local and regional blocks, etc.).

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References

[1] Journavx FDA label. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/219209Orig1s000lbl.pdf. (Accessed on 03/05/2025)

[2] FDA Other Review(s). Available at: https://www.accessdata.fda.gov/drugsatfda_docs/nda/2025/219209Orig1s000TOC.cfm. (Accessed on 03/05/2025)

- [3] Jones J, Correll DJ, Lechner SM, Jazic I, Miao X, Shaw D, Simard C, Osteen JD, Hare B, Beaton A, Bertoch T, Buvanendran A, Habib AS, Pizzi LJ, Pollak RA, Weiner SG, Bozic C, Negulescu P, White PF; VX21-548-101 and VX21-548-102 Trial Groups. Selective Inhibition of NaV1.8 with VX-548 for Acute Pain. N Engl J Med. 2023 Aug 3;389(5):393-405. doi: 10.1056/NEJMoa2209870. PMID: 37530822.