Iowa PDL New Drug Review

Proprietary Name: Journavx®
Common Name: suzetrigine
PDL Category: Analgesics

Pharmacology/Usage: Suzetrigine, the active ingredient of Journavx®, is a sodium channel blocker. Specifically, it is a selective blocker of the $Na_v1.8$ voltage-gated sodium channel, compared to other known voltage-gated sodium channels ($Na_v1.1$ through 1.9). $Na_v1.8$ is expressed in peripheral sensory neurons including dorsal root ganglion neurons, where its role is to transmit pain signals (action potentials). By selectively inhibiting $Na_v1.8$ channels, suzetrigine inhibits transmission of pain signals to the spinal cord and brain. M6-SUZ, a major active metabolite, is a less potent inhibitor of $Na_v1.8$ than suzetrigine by 3.7-fold.

Indication: For the treatment of moderate to severe acute pain in adults.

There is no pregnancy category for this medication; however, the risk summary indicates that there are no available data on use during pregnancy to assess for a drug-associated risk of major birth defects, miscarriage, or other adverse maternal or fetal outcomes. The safety and efficacy of use have not been established in the pediatric population.

Dosage Form: Film-Coated Tablets: 50mg.

Swallow tablets whole, and do not chew or crush.

Recommended Dosage: The recommended starting dose is 100mg by mouth. Take the starting dose on an empty stomach at least 1 hour before or 2 hours after food to avoid delay in onset of action. Clear liquids may be consumed during this time (e.g., water, apple juice, vegetable broth, tea, black coffee).

Starting 12 hours after the initial dose, take 50mg of Journavx® orally every 12 hours. Take these doses with or without food.

Use Journavx® for the shortest duration, consistent with individual patient treatment goals. Use of Journavx® for the treatment of moderate to severe acute pain has not been studied beyond 14 days.

Avoid food or drink containing grapefruit during Journavx® treatment.

Journavx® has not been studied in patients with renal impairment of eGFR <15ml/min. Avoid the use of Journavx® in patients with renal impairment of eGFR <15ml/min. The recommended dosage in patients with eGFR >15ml/min is the same as those with normal kidney function.

Journavx® has not been studied in patients with severe hepatic impairment. Avoid use of Journavx® in patients with severe hepatic impairment. The recommended Journavx® dosage is lower in patients with moderate hepatic impairment than those with normal hepatic function. In moderate hepatic impairment, the recommended starting dose is 100mg orally, on an empty stomach at least 1 hour before or two hours after food. Starting 12 hours after the initial dose, take 50mg orally every 12 hours, with or without food (doses 2, 3, and 4). Starting 12 hours after dose 4, take 50mg orally every 24 hours (dose 5 and subsequent doses). Take these doses with or without food. The recommended dosage in patients with mild hepatic impairment is the same as those with normal hepatic function.

For patients on the standard recommended dosing schedule and if a dose is missed, take the missed dose as soon as possible and then take the next scheduled dose at the recommended time. If two or more doses are missed, take 100mg and then take the next scheduled dose at the recommended time.

For patients with moderate hepatic impairment or patients taking moderate CYP3A inhibitors, if a dose is missed, take the missed dose as soon as possible. If the next scheduled dose is within 6 hours, skip the next scheduled dose, and take the subsequent doses at the recommended time.

Drug Interactions: Suzetrigine and M6-SUZ are CYP3A substrates. Concomitant use of Journavx® with strong CYP3A inhibitors is contraindicated.

When Journavx® is administered to patients taking moderate CYP3A inhibitors, reduce the Journavx® dose. In this situation, the recommended starting dose is 100mg. Take this starting dose on an empty stomach at least 1 hour before or 2 hours after food. Starting 12 hours after the initial dose, take 50mg every 12 hours for doses 2, 3, and 4. Take these doses with or without food. Starting 12 hours after dose 4, take 50mg every 24 hours, with or without food (dose 5 and subsequent doses).

Avoid concomitant use of Journavx® with strong and moderate CYP3A inducers.

If Journavx® is used concomitantly with sensitive CYP3A substrates or CYP3A substrates where minimal concentration changes may lead to loss of efficacy, refer to the prescribing information for the CYP3A substrates for dosing instructions. Dosage modification of the concomitant CYP3A substrates may be required when starting or discontinuing Journavx®.

Journavx® did not result in clinically significant changes in the pharmacokinetics of ethinyl estradiol and levonorgestrel when used concomitantly with an oral contraceptive containing ethinyl estradiol and levonorgestrel. Journavx®-treated patients using hormonal contraceptives containing progestins other than levonorgestrel and norethindrone should use additional nonhormonal contraceptives (such as condoms) or use alternative contraceptives (such as a combined oral contraceptive containing ethinyl estradiol as the estrogen and levonorgestrel or norethindrone as the progestin, or an intrauterine system) during Journavx® treatment and for 28 days after discontinuation of Journavx®.

Box Warning: There is no box warning listed with this product.

Common Adverse Drug Reactions: *Listed % incidence for adverse drug reactions= reported % incidence for drug (Journavx®) minus reported % incidence for placebo. Please note that an incidence of 0% means the incidence was the same as or less than placebo.* The most frequently reported adverse events included pruritus (0.5%), muscle spasms (0.8%), increased blood creatine phosphokinase (0.6%), rash (0.6%).

Listed % incidence for adverse drug reactions= reported % incidence for drug (Journavx®) minus reported % incidence for hydrocodone/acetaminophen 5/325mg. Please note that an incidence of 0% means the incidence was the same as or less than comparator. The most frequently reported adverse events included pruritus (0%), muscle spasms (0.6%), increased blood creatine phosphokinase (0.3%), rash (0.4%).

In trial 1, the incidence of patients who experienced either nausea or vomiting was 20% in the Journavx®-treated patients, 33% in the hydrocodone/acetaminophen-treated patients, and 25% in the placebo-treated patients. In trial 2, the incidence was 9%, 16%, and 12%, respectively.

Contraindications: Concomitant use of Journavx® with strong CYP3A inhibitors is contraindicated.

Manufacturer: Vertex Pharmaceuticals Inc.

Analysis: The efficacy of Journavx® in the treatment of moderate to severe acute pain in adults was established in two randomized, double-blind, placebo- and active-controlled trials of post-operative acute pain, one following full abdominoplasty (trial 1) and the other following bunionectomy (trial 2) for 48 hours. In each trial, pain intensity was measured using a patient-reported 11-point numeric pain rating scale (NPRS), ranging from 0 to 10, where zero corresponds to no pain and 10 corresponds to the worst pain imaginable.

Patients were eligible for study participation if they had moderate to severe pain on the verbal categorical rating system (VRS) and a pain score of ≥4 on the NPRS, within 4 hours of the abdominoplasty completion (trial 1) or during the 9-hour period after discontinuation of regional anesthesia following bunionectomy (trial 2). Once patients became eligible, patients were randomized to receive oral Journavx®, placebo, or hydrocodone bitartrate/acetaminophen (HB/APAP) for a duration of 48 hours. For the Journavx® treatment regimen, patients received an initial loading dose of 100mg, followed by 50mg every 12 hours. For the HB/APAP-control regimen, patients received 5/325mg every 6 hours. With both studies, 400mg of ibuprofen every 6 hours, as needed for pain relief, was allowed as a rescue medication.

Trial 1 assessed the efficacy of Journavx® over 48 hours in adults (N=1,118) with moderate to severe acute pain following a full abdominoplasty procedure. Patients were randomized to Journavx® (N=447), placebo (N=223) or HB/APAP (N=448). Most patients included in this trial were female (98%), while the mean age was 42 years (range 18 to 69). In addition, the study population consisted of 70% who were white, and the mean pain score at baseline was 7.4. In this study, 89% of patients in the Journavx® group completed the treatment period (compared to 75% of patients in the placebo group and 85% in the HB/APAP group), while 9% of patients in the Journavx® group discontinued due to lack of efficacy (compared to 22% in the placebo group and 13% in the HB/APAP group).

Efficacy was assessed by the time-weighted sum of the pain intensity difference from 0 to 48 hours (SPID48) in the Journavx® group compared to the placebo group and then to the HB/APAP group. Results suggested that treatment with Journavx® demonstrated statistically significant superior reduction in pain compared to treatment with placebo. SPID48 results are presented in the table below, which was adapted from the prescribing information.

Note that in an exploratory analysis, the time-weighted sum of the pain intensity difference from 0 to 24 hours (SPID24) reported using the least square mean was 48 for the Journavx® group and 24.2 for the placebo group.

Efficacy Measure	Journavx® (N=447)	Placebo (N=223)	HB/APAP (N=448)
Least Squares (LS) mean	118.4	70.1	111.8
LS mean difference vs placebo; p-value	48.4; p<0.0001		
LS mean difference vs HB/APAP	6.6		

The median time to meaningful pain relief (defined as a ≥2-point reduction in NPRS) was 119 minutes for patients in the Journavx® group and 480 minutes for patients in the placebo group. The median time to onset of perceptible pain relief (defined as a ≥1-point reduction in NPRS) for patients in the Journavx® group was 34 minutes.

Trial 2 assessed the efficacy of Journavx® over 48 hours in adult patients (N=1,073) with moderate to severe acute pain following bunionectomy. Patients were randomized to Journavx® (N=426), placebo (N=216), or HB/APAP (N=431). Most patients were female (85%) and the mean age was 48 years (range 18 to 75 years). The study population included mostly white patients (71%), and the mean pain score at baseline was 6.8 (range 4 to 10). In this trial, 87% of patients in the Journavx® group completed the treatment period (as compared to 82% in the placebo group and 90% in the HB/APAP group), while 12% of patients in the Journavx® group discontinued due to lack of efficacy (as compared to 16% in the placebo group and 8% in the HB/APAP group).

Efficacy was assessed by the time-weighted sum of the pain intensity difference from 0 to 48 hours (SPID48) in the Journavx® group compared to the placebo group and then to the HB/APAP group. Treatment with Journavx® demonstrated statistically significant superior reduction in pain compared to treatment with placebo. SPID48 results are presented in the table below, which was adapted from the prescribing information.

Note that in an exploratory analysis, the time-weighted sum of the pain intensity difference from 0 to 24 hours (SPID24) reported using the least square mean was 30.6 in the Journavx® group and 19.8 in the placebo group.

Efficacy Measure	Journavx® (N=426)	Placebo (N=216)	HB/APAP (N=431)
Least Squares (LS) mean	99.9	70.6	120.1
LS mean difference vs placebo; p-value	29.3; p=0.0002		
LS mean difference vs HB/APAP	-20.2		

The median time to meaningful pain relief (defined as ≥2-point reduction in NPRS) was 240 minutes for patients in the Journavx® group and 480 minutes in the placebo group. The median time to onset of perceptible pain relief (defined as a ≥1-point reduction in NPRS) for patients in the Journavx® group was 60 minutes.

Place in Therapy: Journavx® is a sodium channel blocker indicated for the treatment of moderate to severe acute pain in adults. Use Journavx® for the shortest duration, consistent with individual patient treatment goals. Use of Journavx® for the treatment of moderate to severe acute pain has not been studied beyond 14 days. The efficacy of Journavx® for the treatment of moderate to severe acute pain in adults was established in two randomized, double-blind, placebo- and active-controlled trials of acute post-operative pain, one following full abdominoplasty and the other following bunionectomy. Efficacy for both studies was evaluated by the time-weighted sum of the pain intensity difference from 0 to 48 hours (SPID48) in the Journavx® group compared to the placebo group, and then to the HB/APAP group. Results suggested that treatment with Journavx® demonstrated statistically significant superior reduction in pain compared to placebo in both studies. Per the full text study by Bertoch et al[2], neither study attained the first key secondary endpoint of superiority of suzetrigine as compared with HB/APAP on SPID48. No data is available for long-term safe and effective use.

Summary

There is evidence that Journavx® is more effective than placebo in reducing acute post-operative pain, but not better than the lowest dose of hydrocodone/acetaminophen (an opioid) indicated for acute pain.[3] Therefore, Journavx® should be available without prior authorization as a non-opioid alternative for acute pain, with up to a 14-day quantity limit for safety. No data is available for long-term safe and effective use.

PDL Placement: ☐ **Non-Preferred**
☒ **Preferred (14-day supply limit per 60 days)**

References

[1] Journavx [package insert]. Boston, MA: Vertex Pharmaceuticals, Inc; 2025.
[2] Bertoch T, D'Aunno D, McCoun J, et al. Suzetrigine, a non-opioid Na_V 1.8 inhibitor for treatment of moderate-to-severe acute pain: Two phase 3 randomized clinical trials. *Anesthesiology.* 2025; 142(6): 1085-1099.
[3] American College of Emergency Physicians (ACEP): A joint policy statement of the ACEP, the American Academy of Emergency Nurse Practitioners, the Emergency Nurses Association, and the Society of Emergency Medicine Physician Assistants. Optimizing the treatment of acute pain in the emergency department. Updated April 2017. Accessed March 2025. https://www.acep.org/patient-care/policy-statements/optimizing-the-treatment-of-acute-pain-in-the-emergency-department

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